REMARKS

This paper is submitted in response to the pending Office Action mailed on March 8, 2006. Because this Response is submitted with a certificate of mailing in compliance with 37 C.F.R. §1.8 on or before the shortened period for reply set to expire on **June 8, 2006**, this Response is timely filed.

I. INTERVIEW SUMMARY

Applicants wish to thank Examiner Sirmons for the help and cooperation afforded Applicants' representative Matthew T. Ridsdale, Reg. No. 56,832, during their personal interview conducted on April 25, 2006 (a copy of the PTOL-413 Interview Summary is attached herewith). Applicants' representative and Examiner Sirmons discussed the provided amendments and the pending rejections based, at least in part, on U.S. Patent No. 5,141,493 to Jacobsen et al. Applicants' representative and Examiner Sirmons agreed that the proposed amendments appeared to be patentable over cited references or any modification thereof, and clarify the subject matter originally presented and inherent to these pending claims. In light of these clarifying amendments and the remarks presented herein, Applicants submit that claims 1 to 30 are now in condition for allowance.

II. INFORMATION DISCLOSURE STATEMENT

The Office Action requests that English language translations be provided for: (1) WO 00/20052; (2) JP 10-85324, (3) SU 1344362 and (4) WO 97/47337. Applicants provide and enclose translations of the requested references. Moreover, Applicants submit that, to the best of Applicants' knowledge, these translations represent true and accurate translations of the subject matter disclosed in references 1 to 4.

III. STATUS OF THE CLAIMS

Prior to this response, claims 1 to 65 were pending, with claims 31 to 65 having been withdrawn pursuant to the Restriction Requirement mailed on September 13, 2004. By this response, claims 1, 13 and 24 have been amended, withdrawn claims 31 to 65 have been canceled without disclaimer and no new claims have been added. Thus, claims 1 to 30 remain pending and at issue in this

application. Applicants expressly reserve the right to prosecute and argue the patentability of canceled claims 31 to 65 in one or more related applications.

While Applicants believe that no additional fees are due in connection with this application, Applicants direct and authorize that **Deposit Account No. 02-1818** be charged for any fees deemed owed during the pendency of this application, excluding the issue fee.

IV. CLAIMS REJECTIONS

The Office Action rejects claims 1 to 30 as obvious over U.S. Patent No. 5,141,493 to Jacobsen et al. ("*Jacobsen*") in view of U.S. Patent No. 6,254,567 to Treu et al. ("*Treu*").

In light of the amendments presented herein, and the discussions summarized in Section I, Applicants submit that the amended claims 1 to 30 are not rendered obvious by *Jacobsen,* either alone or in combination with *Treu.* In particular, *Jacobsen* discloses and requires the use of primary and second circuits coupled by a dialyzer 24. *See* FIGS. 1A and 1B Neither *Jacobsen* nor *Treu* discloses or even suggests a single loop that operates, or can operate, at different feed, circulation and discharge rates. Thus, *Jacobsen* and *Treu* either alone or in combination do not teach or suggest each and every element recited in the claims and, as a result, cannot provide the basis for establishing a *prima facie* case of obviousness. For at least this reason, Applicants submit that claims 1 to 30 are patentable over these references or any combination thereof.

V. CONCLUSION

For the foregoing reasons, Applicants respectfully submit that the present application is in condition for allowance and earnestly solicit reconsideration of same.

Respectfully submitted,

BELL, BOYD & LLOYD LLC

BY: _____

Matthew T. Ridsdale
Reg. No. 56,832
Cust. No. 29200
Direct: (312) 807-4440
mridsdale@bellboyd.com

Dated: **May 4, 2006**

Interview Summary	Application No.	Applicant(s)	
	10/624,150	CHILDERS ET AL.	
	Examiner	Art Unit	
	Kevin C. Sirmons	3767	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Kevin C. Sirmons*. (3)_____.

(2) *Matt Ridsdale*. (4)_____.

Date of Interview: *25 April 2006*.

Type: a)☐ Telephonic b)☐ Video Conference
c)☒ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: *1*.

Identification of prior art discussed: *Jacabsen et al U.S. Pat. No. 5,141,493*.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Applicant and the examiner agreed that "consisting of only a single loop" may overcome the prior art of record.* .

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

KEVIN SIRMONS
PRIMARY EXAMINER

Kevin C. Sirmons

Examiner's signature, if required

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

DEVICE AND METHOD FOR PERFUSING PERITONEAL DIALYZING FLUID

Patent number:	WO0020052
Publication date:	2000-04-13
Inventor:	SAKAI ASAHI (JP)
Applicant:	SAKAI ASAHI (JP)
Classification:	
- international:	***A61M1/28;*** **A61M1/28;** (IPC1-7): A61M1/28
- european:	A61M1/28
Application number:	WO1999JP05535 19991007
Priority number(s):	JP19980285029 19981007

Also published as:

EP1121948 (A1)
US6666842 (B1)
JP2000107286 (A)
CA2346369 (A1)
EP1121948 (B1)

more >>

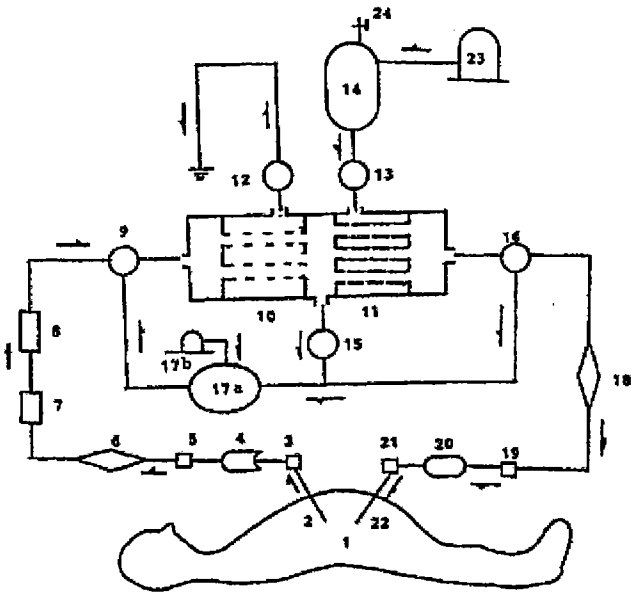
Cited documents:

WO9747337
EP0112104

Report a data error here

Abstract of **WO0020052**

A perfusing device which is used in a peritoneal dialyzing method and which re-utilizes as an osmotic pressure agent protein components eluted from the interior of the body into a peritoneal dialyzing fluid, keeps a circulating circuit sterile and improves a water removing efficiency and a dialyzing/removing efficiency of uremigenic substances, the device comprising a pre-filter, a first filter having a translucent membrane with a maximum permeable molecule of up to 30,000 daltons, a pump for reducing a pressure outside the first filter circuit to below that inside the circuit, a second filter having a translucent membrane with a maximum permeable molecule of up to 5,000 daltons and a pump for pressurizing a replenishing fluid outside the second filter circuit, the peritoneal dialyzing fluid perfusing device automatically infusing/discharging liquid through a catheter indwelling in a human abdominal cavity; and a perfusing method. Prevention of protein denaturation implemented by the above arrangement can minimize contacts with an outside air and foreign matters and circulating circuit clogging, and completely prevent entry of external pathogenic bacteria and endotoxins.



US006666842B1

(12) **United States Patent**
Sakai

(10) **Patent No.: US 6,666,842 B1**
(45) **Date of Patent: Dec. 23, 2003**

(54) **DEVICE AND METHOD FOR PERFUSING PERITONEAL DIALYZING FLUID**

(76) Inventor: **Asahi Sakai**, 4-8, Hachimandai 1-Chome, Sakura-Shi, Chiba 285-0867 (JP)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/806,686**

(22) PCT Filed: **Oct. 7, 1999**

(86) PCT No.: **PCT/JP99/05535**

§ 371 (c)(1),
(2), (4) Date: **Apr. 4, 2001**

(87) PCT Pub. No.: **WO00/20052**

PCT Pub. Date: **Apr. 13, 2000**

(30) **Foreign Application Priority Data**

Oct. 7, 1998 (JP) 10-285029

(51) **Int. Cl.**[7] **A61M 1/00**; A61M 37/00; C02F 9/00; B01D 11/00; B01D 61/00

(52) **U.S. Cl.** **604/29**; 604/5.01; 210/645; 210/651; 210/195.2

(58) **Field of Search** 604/29, 4.01, 5.01, 604/5.04, 6.09, 6.11, 6.13, 93.01, 113, 131, 151, 264, 272, 523; 210/644, 645, 646, 649, 650, 651, 767, 175, 181, 194, 195.2, 348, 439, 500.1

(56) **References Cited**

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5,141,493 A * 8/1992 Jacobsen et al. 604/29
5,498,338 A * 3/1996 Kruger et al. 210/641
5,660,722 A 8/1997 Nederlof
6,254,567 B1 * 7/2001 Treu et al. 604/29

* cited by examiner

Primary Examiner—Brian L. Casler
Assistant Examiner—Mark K Han
(74) *Attorney, Agent, or Firm*—Wenderoth, Lind & Ponack, L.L.P.

(57) **ABSTRACT**

An instrument for continuous recirculation of peritoneal dialysate to infuse and drain out the dialysate automatically through catheters implanted in a peritoneal cavity of a human body. The instrument includes a prefilter, a primary filter comprising a semipermeable membrane having a maximum permeable molecule of up to 30,000 dalton, a pump for lowering the outside pressure of the primary filter relative to the inside pressure, a secondary filter having a semipermeable membrane having a maximum permeable molecule of 5,000 dalton, a pump for raising the pressure of a supplemental liquor line relative to the inside of a secondary filter line, and a method of recirculating dialysate using the above-mentioned instrument. The recirculation instrument permits the reuse of protein which is permeated out from a patient's body, as an osmotic agent in peritoneal dialysate, in order to maintain a disinfected recirculating line, and to improve an ultrafiltration rate and clearance of uremic toxin.

7 Claims, 4 Drawing Sheets

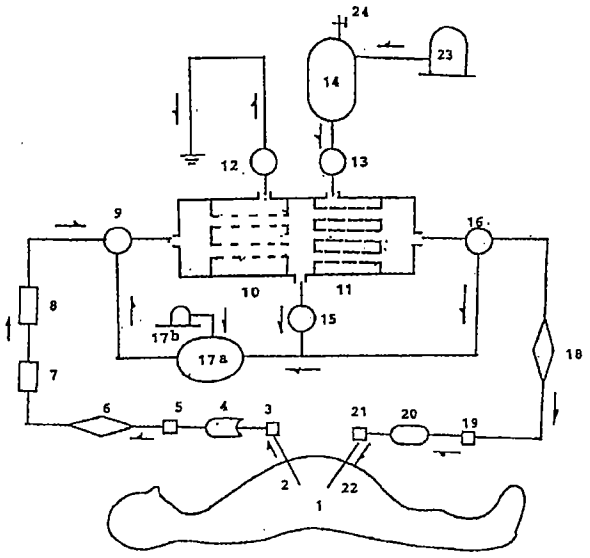
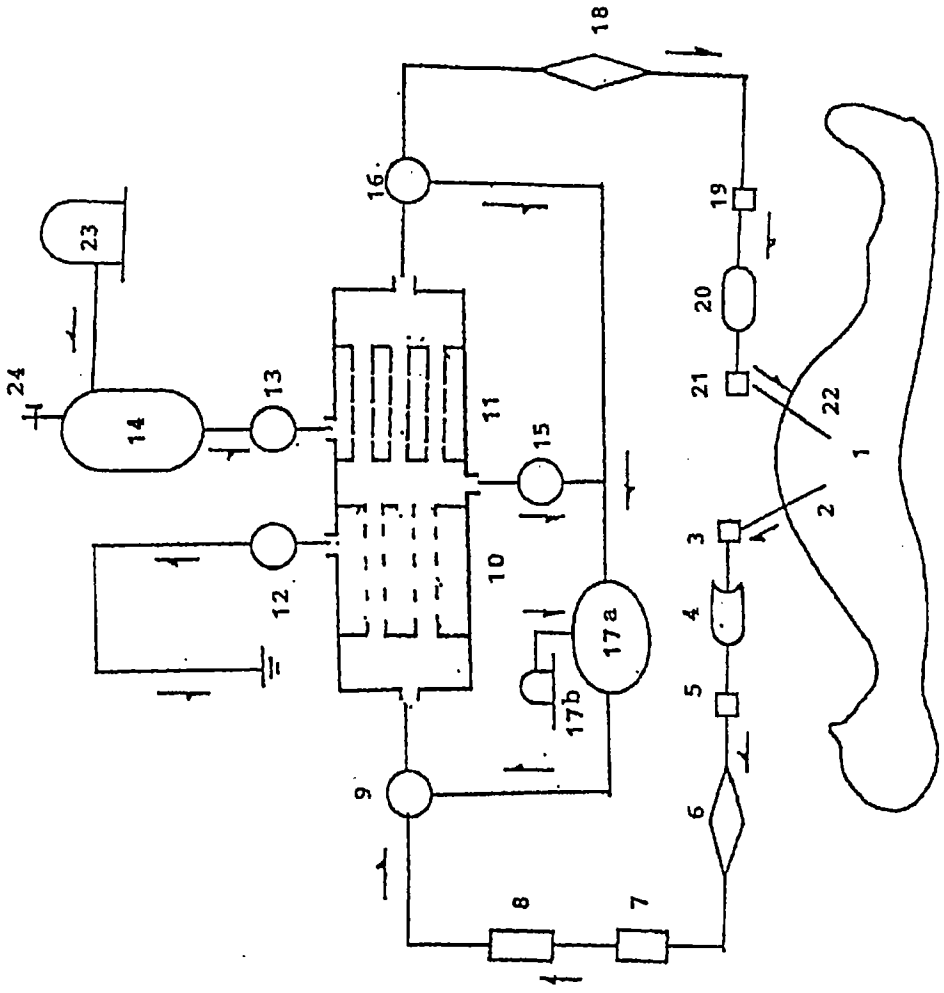


Fig.1



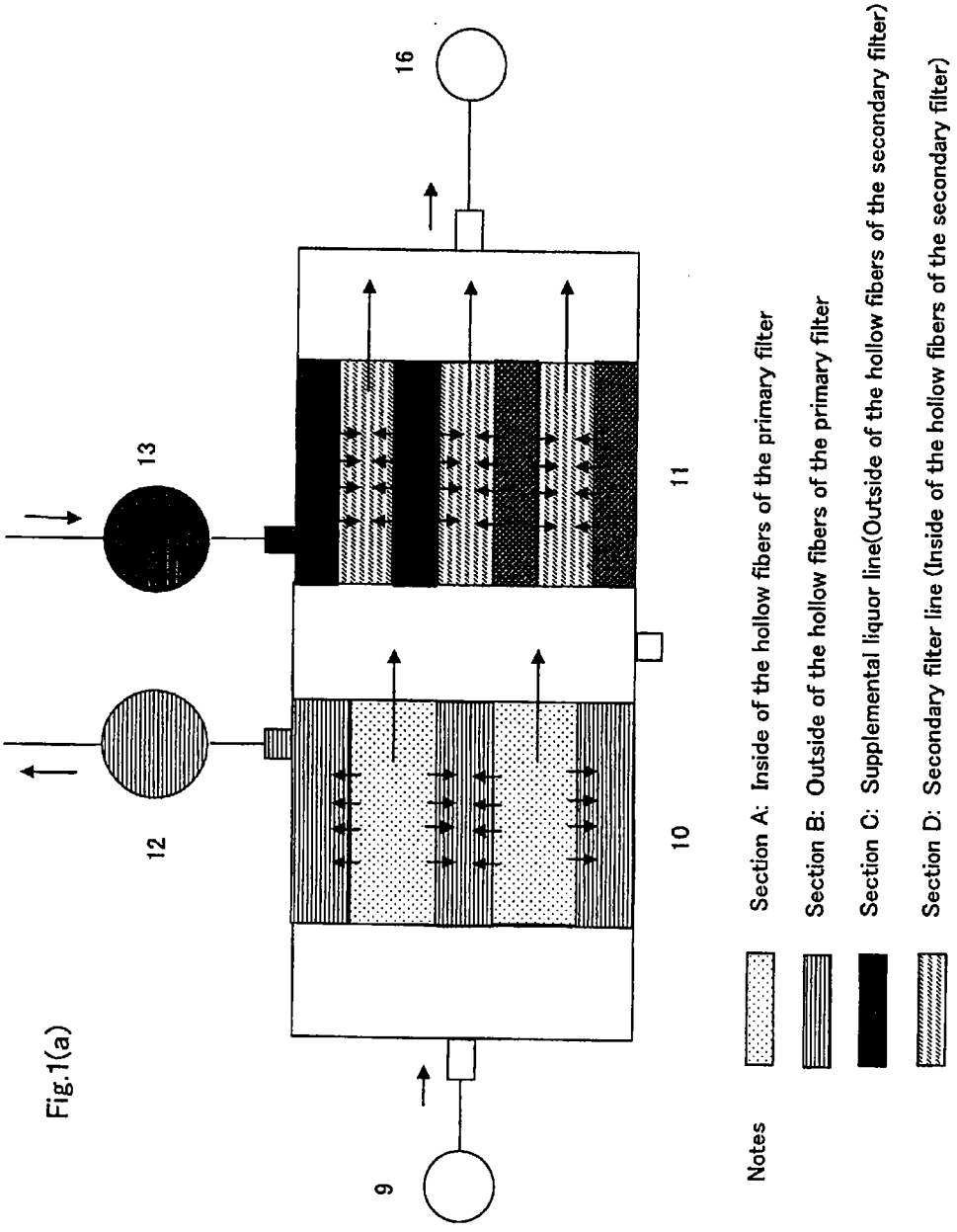

16
13
11
12
10
9
Notes
Section A: Inside of the hollow fibers of the primary filter
Section B: Outside of the hollow fibers of the primary filter
Section C: Supplemental liquor line(Outside of the hollow fibers of the secondary filter)
Section D: Secondary filter line (Inside of the hollow fibers of the secondary filter)

Fig.1(a)

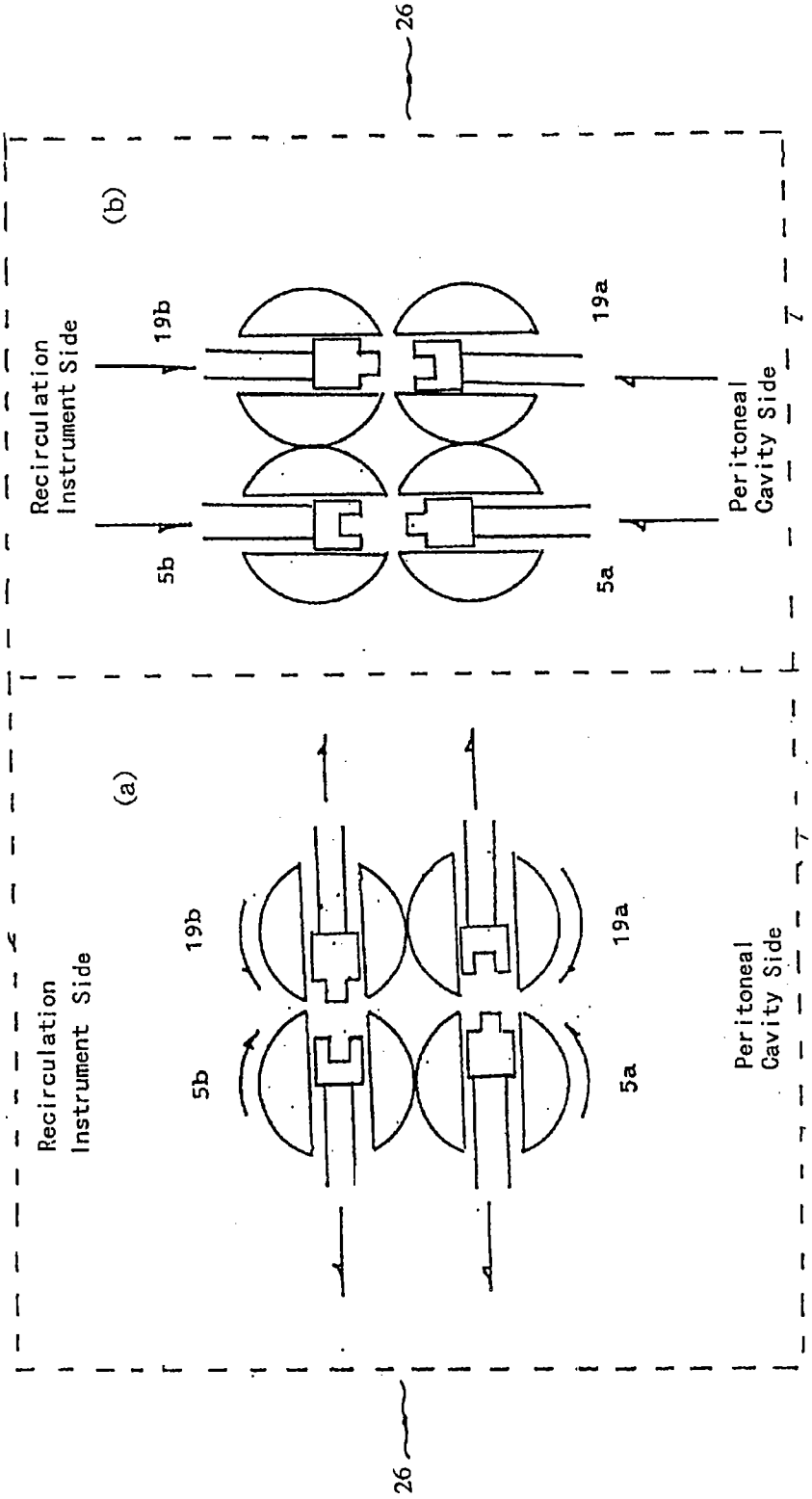
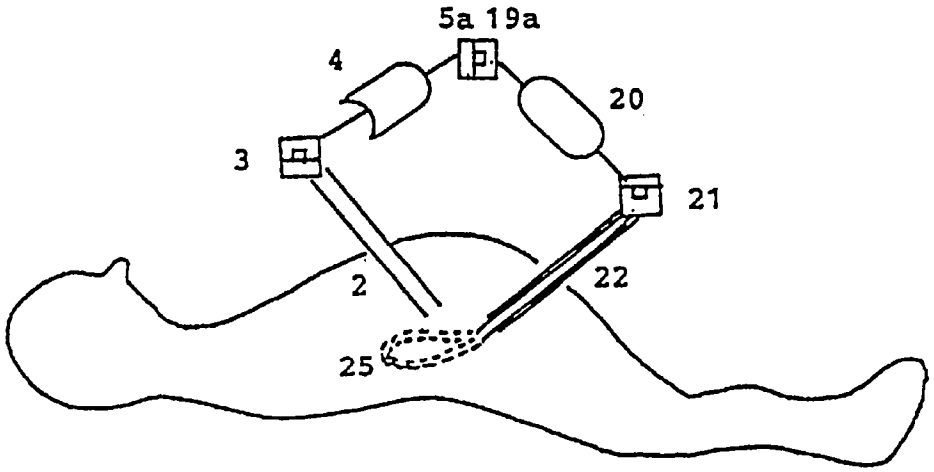

26
(b)
Recirculation Instrument Side
19b
19a
5b
5a
Peritoneal Cavity Side
(a)
Recirculation Instrument Side
19b
19a
5b
5a
Peritoneal Cavity Side
26

Fig.2

Fig.3



DEVICE AND METHOD FOR PERFUSING PERITONEAL DIALYZING FLUID

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a peritoneal dialysis instrument for improving dialysis efficacy in removing excess liquid and uremic toxin by maintaining polymer osmotic agents in place of glucose in a recirculation line without requiring outside contact for the therapy of chronicle renal failure disease.

2. Description of the Related Art

Peritoneal dialysis has been applied as an effective therapy for renal failure patients. The dialysis is performed so that dialysate is infused into the peritoneal cavity from the dialysate bag through a catheter, which is implanted in the patient's peritoneal cavity, and the dialysate is stored in the cavity for a certain time. Then, the dialysate is drained out through the same catheter. This procedure is repeated a few times a day.

This dialysis has a few advantages over hemodialysis from a physiological point of view, as it purifies blood continuously through the patients' peritoneum, while hemodialysis uses artificial membranes. Also, peritoneal dialysis enables the patients to participate in social activity, and as a result, the dialysis has been widely applied.

In hemodialysis, ultrafiltration is achieved by raising the pressure of the blood line over that of the dialysate line. However, the same method can not be applied to peritoneal dialysis. As a result, an osmotic agent is added into the dialysate so as to raise the osmotic pressure of the dialysate over that of plasma, and the dialysate is infused into the peritoneal cavity so as to contact it to the peritoneum for removing excess liquid from the patient's body. For this purpose, glucose has been used as an osmotic agent. However, adverse effects such as the disfunctioning of the, peritoneum due to the absorption of such a large quantity of the osmotic agent into the patient body are now recognized as a serious problem.

For solving the aforementioned problem, the inventor of the present invention has proposed an instrument and a method by which serum protein, such as albumin, globulin and the like which are permeated out through peritoneum into the dialysate, is recovered and refined, and is then concentrated and reused with dialysate as the most physiological substitutes of glucose.

In these proposed processes, the following were disclosed:

(A) A method to dissolve the recovered and refined protein in dialysate after which low molecular weight uremic toxin substances not higher than 30,000 daltons are removed by the repeated concentration/dilution procedures with a semipermeable membrane, and to reuse it as a substitute of glucose. (Japanese Laid Open Patent Application Hei 9-327511)

(B) A method to keep the abovementioned device and the components disinfected. (Japanese Laid Open Patent Application Hei 10-85324)

(C) A method to separate the malignant solute in the solvent and refine the protein by acidifying the protein and then de-acidifying it through water dialysis so as to deposit it at iso-electric pH (Japanese Laid Open Patent Application Hei 9-302388)

Also, for carrying out the invention (C), it was disclosed that the device comprises the followings:

(D) An inflow line having a filter whose maximum pore size is 100–300 nanometers for preventing bacteria invasion into the peritoneal cavity; and

(E) A two step prefilter having a pore size between 5 and 200 microns to remove blood cells, peritoneum mesothelial cells, fibrin and the like suspended in the effluent when it is drained out from peritoneal cavity.

A few attempts have been reported to utilize serum protein in ascites (Hwang, E. R., Richard, D. O. Sherman, A. et al., Dialytic Ascites Ultra-filtration in Refractory Ascites, Am. J. Gastroenteral, 77(9): 652–654, 1982, for example)

However, they did not refer to removing uremic toxin, because their target was not a renal failure patient.

Also, a method to add a peritoneum protecting component of a molecular weight of not higher than 3,000 daltons recovered from peritoneal dialysis effluent into dialysate (Japanese Laid Open Patent Application Hei 8-337590). However the recovery and reuse of the component of the molecular weight higher than 3,000 daltons is not suggested.

When plasma protein that is permeated out of the patient body is reused as an osmotic agent in place of glucose, the following conditions need to be satisfied:

(I) To minimize the contact with atmosphere and foreign matters so as to not denature the protein;

(II) To minimize plugging the semi-permeable membrane on the recirculation line, and to decrease the frequency of exchange; and

(III) To completely prevent the invasion of pathogenic bacteria and endotoxin.

For the solution of the aforementioned (I) problem, it may be suggested that a filter is set at the exit of the catheter, or, as a further perfect protection, a hollow fiber type semi-permeable membrane is set in a peritoneal cavity in order to keep the polymer in the peritoneal cavity. However, in those cases, complicated preventive means are required to avoid plugging of the membrane, and the exchange of the filter requires skillful care.

SUMMARY OF THE INVENTION

The present invention has developed a practical method and an instrument for solving the aforementioned problems, by the combination of either one of the following technologies:

[I] The drained dialysate is warmed up to a preset temperature, and then it is filtered through a prefilter for removing foreign materials so as to prevent the plugging of the filter.

[II] A semi-permeable membrane (having a cut-off point of up to 30,000 dalton) filter is used for removing uremic toxin of low molecular weight and of middle molecular weight.

[III] A supplemental electrolyte solution is supplied through a semi-permeable membrane filter (having a cut-off point of up to 5,000 dalton) for preventing the infection and invasion of endotoxin.

Also, the present inventor has found that by the use of the device, dialysate may be drained out of the peritoneal cavity and may be recirculated in a closed line. In addition, a portion of the dialysate may be filtered out through a semi-permeable membrane to remove malignant component, and then, a fresh dialysate may be supplemented through a semipermeable membrane and returned automatically into the peritoneal cavity.

Briefly, the present invention relates to an instrument-that comprises (a) a prefilter, (b) a first filter that comprises a semi-permeable membrane having a maximum permeable

molecule of up to 30,000 dalton, (c) a pump to lower the outside pressure of the first filter (b) relative to the inside pressure, (d) a second filter that comprises a semi-permeable membrane having a maximum permeable molecule of 5,000 dalton, (e) and a pump to raise the pressure of a supplemental liquor line relative to the inside line of the second filter.

Also, the present invention relates to a method characterized in that dialysate is drained out of the peritoneal cavity and recirculated in a closed line, and a portion of the dialysate is filtered out through a semi-permeable membrane. Then, an equivalent volume of fresh dialysate is supplemented through a semi-permeable membrane having a maximum permeable molecule of 5,000 dalton and is then returned into the peritoneal cavity.

As a favorable embodiment for carrying out the present invention, the following technologies may be adapted:

(1) A bacteria-free filter (having a maximum pore size of 100–300 nanometers) is set up on the peritoneal cavity side of the inflow line's joint.

(2) Dialysate in the peritoneal cavity is recirculated through a perfectly closed and continuously connected and previously disinfected line for keeping the protein not denatured in the automatic dialysate recirculation instrument.

(3) A reverse flow prevention valve (anti-reverse flow valve) is set up on the withdrawn line.

(4) A closed chamber, of which the inside can not directly be contacted by fingers, is set up for disconnection and connection procedure by remote operation from outside, after the infusion of dialysate for the daytime cycle before getting up in the morning.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** illustrates a Peritoneal Dialysate Recirculation Circuit in a nighttime state where the peritoneal dialysate recirculation instrument is connected with the patient's outflow and inflow catheters, respectively, and the dialysate is recirculated.

FIG. **1**(*a*) is an enlargement of the structure of the primary filter and the secondary filter of FIG. **1** and illustrates the flow of the dialysate and a supplemental solution therethrough.

FIG. **2** illustrates an exchanging method of an outflow line joint and an inflow line joint for:

(a) a disconnecting operation of the joint, which has been directly connected in the daytime (FIG. **3**), and a rotation operation of the parts; and

(b) a rotating operation of the disconnected part so as to face the part of peritoneal cavity side and the part of recirculation instrument side, and a connecting operation of the parts so as to make ready for nighttime recirculation (FIG. **1**).

FIG. **3** illustrates an O-shaped circuit of the catheter at an extracorporeal side (during a daytime state when the patient leaves and is away from the recirculation instrument for daily life) and hollow fibers in the peritoneal cavity.

EXPLANATION OF THE REFERENCE NUMERALS

1. Peritoneal Cavity
2. Outflow Catheter
3. Joint
4. Anti-Reverse Flow Valve
5. Outflow Line Joint
5*a*. Patient Peritoneal Cavity Side Terminal of Outflow Line Joint
5*b*. Recirculation Instrument Side Terminal of Outflow Line Joint
6. Heater
7. Prefilter
8. Bacteria-free Filter
9. Pump
10. Primary Filter
11. Secondary Filter
12. Suction Pump
13. Feeding Pump
14. Supplemental Solution Vessel
15. Pump
16. Pump
17*a*. Container
17*b*. Reservoir of Osmotic Agents
18. Warmer
19. Inflow Line Joint
19*a*. Patient Peritoneal Cavity Side Terminal of Inflow Line Joint
19*b*. Recirculation Instrument Side Terminal of Inflow Line Joint
20. Bacteria-free Filter
21. Joint
22. Inflow Catheter
23. Reverse Osmosis Membrane Water
24. Inlet Valve of Chemicals
25. Loupe-shape Hollow Fibers
26. Isolated Case

DETAILED DESCRIPTION OF THE INVENTION

The present invention will be explained with reference to FIG. **1**.

FIG. **1** illustrates an outflow catheter **2** and an inflow catheter **22** in a peritoneal cavity **1**.

It happens to be observed often that when liquor is recirculated from an inflow entrance to an outflow exit at a consistent rate, a localized flow, a so-called channeling, is formed in the peritoneal cavity; then, a portion of the liquor tends to stay at "dead spaces". For solving this problem, a certain number of loop-shaped porous hollow fibers **25** are fixed at the end of the inflow catheter so that the dialysate may flow throughout the cavity as illustrated in FIG. **3**. Instead of an outflow catheter **2**, an outer lumen of a concentric double lumen catheter may alternatively be used.

Outflow catheter **2** comprises joint **3**, anti-reverse flow valve **4**, and outflow joint **5**, and the flow catheter is connected with heater **6** and prefilter **7** in series.

Outflow joint **5** comprises peritoneal side part **5***a* and instrument side part **5***b*, as illustrated in FIG. **3**. During recirculation time, which occurs at night, the parts **5***a* and **5***b* are connected together. The joint **5** has the structure of male/female parts, which are directly adaptable to each counterpart of inflow joint **19**, as is discussed further below. During the daytime, which is when dialysate is not recirculated but is stored in the peritoneal cavity, the joint part **5***a* is connected with the joint part **19***a*, and the joint part **5***b* is connected with the joint part **19***b*, thereby forming the circuit illustrated in FIG. **3**.

The dialysis effluent that is drained out of the patient's peritoneal cavity contains peritoneum mesothelium cells, leucocyte cells, deposited fibrin, and the like. These foreign particles may be separated from the filtrate with prefilter **7**.

Fibrinogen in the dialysate effluent tends to be deposited out as fibrin after prefiltration, and it plugs the filter. This has

often been experienced when plasma and humor is filtered. For preventing the plugging problems, it is desirable to warm up the effluent up to 55–60° C. by means of a heater before prefiltration.

After the dialysate is passed through a bacteria-free filter **8**, it is flown by pump **9** to the first filter **10** and then to the second filter **11**. The first filter has a semi-permeable membrane of a maximum permeable molecule of up to 30,000 dalton, greater than that of 2-microglobulin, for example. By filtering out a portion of the dialysate through this filter, middle molecule malignant components, such as a 2-microglobulin of the molecular weight of 11,800 daltons, may be removed.

After filtering through the first filter, the partially filtered dialysate is supplemented with a supplemental electrolyte solution. The supplemental solution is added through the second filter whose semipermeable membrane does not pass endotoxin. The second filter has a semipermeable membrane of a maximum permeable molecule of up to 5,000 dalton so that it can prevent invasion of bacteria and endotoxin.

Endotoxins are lipopolysaccharides, of which the largest ones have a molecular weight of a few hundred thousand dalton. The smallest lipopolyssaccharides have a molecular weight of 6,000–8,000 dalton. On the other hand, supplemental chemicals and additives are lighter molecules, such as 1,000 dalton, so that they may pass through this semipermeable membrane of the second filter **11**.

Due to the reduced pressure in the outside of the first filter **10** by suction pump **12**, dialysate in the first filter **10** is suctioned out. The supplement solution in the second filter is pressed by feeding pump **13** to feed in through the second filter **11**. The filtration in both filters is accelerated by these pumps **12** and **13**.

FIG. 1(*a*) illustrates an enlargement of the structure of the primary filter **10** and the secondary filter **11**, and the flow of the dialysate and the supplemental solution. As shown in FIG. 1(*a*), the primary filter **10** and the secondary filter **11** each comprise a number of hollow fibers. The sections labeled as Section A are inside the hollow fibers which lead the dialysate rightward to the secondary filter **11**. The sections labeled as Section B are outside of the primary filter **10** and lead the suctioned filtrate upward to be discarded by the suction pump **12**. The individual sections of Section B appear to be isolated, but in fact, they are in a continuous space leading to the suction pump **12**. In the suctioned filtrate, middle molecules of less than 30,000 dalton are thereby removed as indicated by the upward arrow from primary filter **10** to the suction pump **12**.

The supplemental solution is stored in a supplemental solution vessel **14**, and it is sent to the second filter by feeding pump **13** as indicated by the downward arrow from the supplemental solution vessel **14** and the supplemental liquor line (sections labeled as section C of the secondary filter **11**) into the secondary filter line (sections D on the inside of the hollow fibers of the secondary filter **11**). Amino acids, fatty acids, glucose, peptides or any mixture thereof are added into the supplemental solution through a line which is connected with a valve **24** that is equipped in the supplemental solution vessel **14**.

The above-mentioned supplemental solution may be:

(a) a commercially available infusion solution or peritoneal dialysate which is sterilized and packed in a supplemental solution vessel **14**, or

(b) a hemodialysis concentrate or dry chemicals for hemodialysis, which is diluted or dissolved with, reverse osmosis water.

After partial filtration in the first filter **10** and supplementation at the second filter **11** the dialysate is flown by pump **16** through a warmer **18**, where it is warmed up to a standard corporeal temperature. Then, the dialysate is infuised through inflow joint **19**, bacteria-free filter **20**, and joint **21** so as to pass into peritoneal cavity **1**.

On the by-pass line **15-17***a*-**9**, a container **17***a* is set up, where a portion of polymer components, which is stored in the peritoneal cavity during the daytime, may be stored. The solution can be circulated through the line by pump **15** so as to repeat the concentration/dilution procedures. A cooling or freezing unit may be equipped for the container **17***a*.

One of the present invention's aims is the reuse of recovered plasma protein permeated from a patient's body through peritoneum into the dialysate.

However, in the case where the recovered protein is not enough to achieve sufficient ultrafiltration, other osmotic agents may be supplemented. Such supplemental agents may be high or low molecular weight substances.

High molecular weight substances maybe oligosaccharides, and low molecular weight substances may be glucose or amino acids. Even when substances whose daily dose is restricted are used, usage is within a tolerable quantity, and those osmotic agents may be used so that the required osmotic pressure can be obtained. Low molecular weight agents are added from a supplemental reservoir **14**, and high molecular weight agents are supplied from an osmotic agent reservoir **17***b* into the container **17***a*, where the additives are mixed with the dialysate.

The recirculation instrument is connected with peritoneal catheters at night so as to automatically achieve peritoneal dialysate recirculation. However, in the daytime, joint **5** and joint **19** are disconnected from the recirculation instrument and form a daytime circuit as illustrated in FIG. **3**. For such a disconnection and connection operation, each joint comprises a respective part a and part b as illustrated in FIG. **2**. That is, joint **5** consists of parts **5***a* (male) and **5***b* (female), and joint **19** consists of parts **19***a* (female) and **19***b* (male). When parts **5***a* and **5***b* are disconnected from each other and parts **19***a* and **19***b* are disconnected from each other, parts **5***a* and **19***a* can be connected and parts **5***b* and **19***b* can be connected as illustrated in FIG. **3**. According to the present invention, outflow joint **5** and inflow joint **19** are set up adjacently in an isolated case **26** and manipulated from outside of the case to be isolated and free from human contact.

By use of the recirculation instrument according to the present invention, extraperitoneal recirculation procedures may be achieved continuously and automatically in the following way. First, before the patient begins sleeping, parts **5***a* and **19***a* and parts **5***b* and **19***b*, which have been respectively connected in the isolated case **26** during the daytime, are disconnected. Then, each part is rotated by 90 degrees to the direction along the arrows as illustrated in FIG. **2**. Then, parts **5***a* and **5***b* are connected, and parts **19***a* and **19***b* are connected to form a recirculating circuit as illustrated in FIG. **1**.

When the circuit line is set up, recirculation is started. After concentrating the drained dialysate and removing uremic toxin in the first filter, a portion of the concentrate is stored in the container **17***a*.

The remaining concentrate is added to a fresh electrolyte solution through the second filter **11**, and then is infused into the peritoneal cavity. If needed, concentrating/diluting procedures are repeated a few times through a circulation circuit (**16-17***a*-**9**). In some cases, an electrolyte solution, such as amino acids, glucose, fatty acids, or peptides, etc., is added.

Not only sodium caprilate and N-acetyltryptophan are added as stabilizers to prevent the recycled protein from becoming denatured, but acids, alkali, and anti-oxidants, such as, glutathione, vitamin C, vitamin E and reductants, are also added to the electrolyte solution so as to release urea, bilirubin, and S—S bonded chemicals that are attached to cysteine, 34th amino acid from N-terminal of albumin. By making albumin as active as those of healthy persons by the abovementioned way before infusing it into the peritoneal cavity, it may thereby improve the therapy effect.

Thus, the dialysate in the peritoneal cavity is consistently drained out, and is substituted partly with a fresh electrolyte solution by the way of recirculation at night when the patient sleeps.

Before getting up in the morning, all or almost all of the dialysate in the peritoneal cavity is drained out, and the drain is repeatedly concentrated and diluted. Then, the aforementioned chemicals are added and infused into the peritoneal cavity. The joints **5** and **19** are disconnected to form a circuit as illustrated in FIG. **3** by directly connecting the corresponding part of joint **5** with the corresponding part of joint **19**. Briefly, as in FIG. **3**, on the catheter side, an "O" shaped circuit is formed. On the catheter side, part **19***a* is connected to a bacteria-free filter entrance **20** on the inflow line, and part **5***a* is connected to an anti- reverse flow-valve exit **4** on the outflow line. On the recirculation instrument side, the counter parts **5***b* and **19***b* are connected.

The above-mentioned operation can be manipulated in a separate case so as to prevent human contact, and through which a continuous recirculation of the dialysate can be performed.

By use of the instrument according to the present invention, continuous recirculation can be achieved simultaneous to a partial substitution of the dialysate.

By the instrument according to the present invention, safely reusing the permeated out protein into the peritoneal dialysate, and continuous recirculation of the dialysate can be achieved in the simplest way. Briefly, every day, dialysate is drained out and infused through a semipermeable membrane, and solution flows through a completely closed circuit line so as to minimize the risk of infection.

By the instrument according to the present invention, continuous recirculation of the dialysate can be achieved simultaneous to a partial substitution. As a result, continuous draining of the dialysate out of the peritoneal cavity and partial substitution of the dialysate with fresh electrolyte solution can be achieved during the nighttime when the patient sleeps. After getting up in the morning, the patient can be disconnected from the instrument and thereafter enjoy a daily life in the daytime without being connected to an external instrument.

It has been said that increasing the number of dialysis cycles per day is effective for improving the dialysance of peritoneal dialysis. However, too many cycles of peritoneal dialysis increases the vacancy time of a peritoneal cavity. To solve this problem, the use of tidal type recirculation has been proposed. However, tidal type recirculation leaves a portion of liquid in the peritoneal cavity, and it can not improve the dialysance significantly.

The present invention, in contrast, can improve the dialysance, as the dialysate recirculates without a vacancy time in the peritoneal cavity. Another recirculating method in which the dialysate is refined by extraperitoneal dialysis by use of an artificial dialyser and extracoporial dialysate can improve the dialysance, but this recirculating method requires a large volume of dialysate. The present invention provides a much more economical dialysis due to a partial substitution of recirculated dialysate. This advantage is also valid in the case where no polymer component is contained and recycled.

Instead of requiring large volumes of dialysate to be delivered, on site preparation of dialysate by diluting the dialysate concentrate or by dissolving dry chemicals is very effective for reducing the cost of therapy. The water preparation device for the dissolution and dilution by reverse osmosis membrane may be equipped in the instrument according to the present invention so as to provide a safe and low cost dialysate.

Infection can be prevented by the use of a previously connected, packed and sterilized extracorporeal recirculation line. Also, the infection rate at a periodical exchange can be significantly reduced by having the outflow and inflow connection parts fixed adjacent to one another in a closed case as illustrated in FIG. **2**, and the connection parts can be disconnected and exchanged by outside manipulation free from contact of the atmosphere and other foreign, e.g. human, contact.

By using the above-described method and instrument, the present invention enables (I) minimizing contact with the atmosphere and other foreign matters such as human contact, (II) minimizing the plugging of the semi-permeable membrane on the recirculation line, and (III) perfectly preventing the invasion of bacterial and endotoxin from external sources.

What is claimed is:

1. An instrument for continuous recirculation of peritoneal dialysate to infuse and drain out the dialysate automatically through catheters implanted in a peritoneal cavity of a human body, said instrument comprising:

a prefilter;

a primary filter located downstream of said prefilter, said primary filter being operable to filter out a portion of the dialysate, and said primary filter comprising a semipermeable membrane having a maximum permeable molecule of up to 30,000 dalton;

a suction pump operable to lower an outside pressure of said primary filter relative to an inside pressure of said primary filter;

a feeding pump operable to supply a fresh dialysate; and

a secondary filter located downstream of said feeding pump, said secondary filter being operable to filter out a portion of the fresh dialysate, and said secondary filter comprising a semipermeable membrane having a maximum permeable molecule of up to 5,000 dalton.

2. The instrument for continuous recirculation of peritoneal dialysate according to claim **1**, wherein a supplemental liquor line provides communication between said feeding pump and said secondary filter.

3. The instrument for continuous recirculation of peritoneal dialysate according to claim **2**, wherein said feeding pump supplies the fresh dialysate to said secondary filter through the supplemental liquor line, said feeding pump being further operable to raise the pressure of the supplemental liquor line relative to an inside pressure of said secondary filter.

4. The instrument for continuous recirculation of peritoneal dialysate according to claim **1**, wherein the instrument is equipped with a dialysate recirculation line that is replaceable, made of flexible material, prefabricated as a continuous line from an outflow terminal to an inflow terminal, and sterilized.

5. The instrument for continuous recirculation of peritoneal dialysate according to claim **4**, further comprising an

outflow joint and an inflow joint which can be directly connectable to each other, and in an isolated case the outflow and inflow joints can be fixed adjacent to each other so that terminals of a recirculation instrument side and terminals of a patient peritoneal cavity side may be disconnected and connected by remote handling free from human contact.

6. The instrument for continuous recirculation of peritoneal dialysate according to claim 1, further comprising an outflow joint and an inflow joint which can be directly connectable to each other, and in an isolated case the outflow and inflow joints can be fixed adjacent to each other so that terminals of a recirculation instrument side and terminals of a patient peritoneal cavity side may be disconnected and connected by remote handling free from human contact.

7. The instrument for continuous recirculation of peritoneal dialysate according to claim 1, wherein said prefilter, which is located upstream of said primary filter, is operable to prevent said primary filter from becoming plugged by cells and fibrin in the dialysate withdrawn from the peritoneal cavity.

* * * * *

(19) Japanese Patent Office (JP)

(11) Publication number

(12) Publication of Patent Applications (A) **JP 10-85324,A**

(43) Publication Date: April 7, Heisei 10 (1998)

(51) Int. Cl.[6] ID Symbol	F I
A61M 1/14 525	A61M 1/14 525
563	563
A61K 35/16	A61K 35/16
A61L 2/02	A61L 2/02 Z
2/12	2/12

Request for examination: Not requested
Number of claims: 8 OL (6 pages total)
Continued to the last page.

(21) Filing Number:
Japanese Patent Application No. 8-248411

(22) Filing Date: September 19, Heisei 8 (1996)

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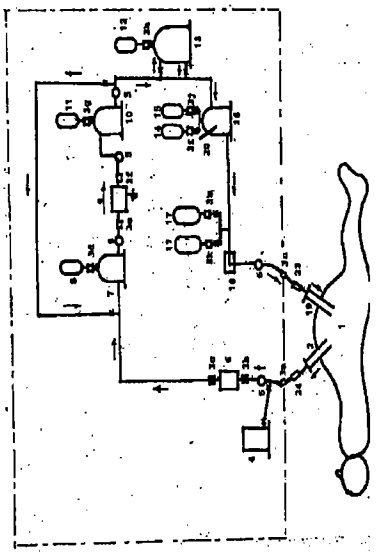
(54) [Title of the Invention]

Sterilization and Disinfection of the Collection/Regeneration Device of Peritoneal Dialysate, and Method of Sterilizing and Preserving the Dialysate

(57) [Abstract]

[Objective] The [purpose of the present invention is] to provide a comprehensive method of sterilizing and disinfecting the device for collection/regeneration of peritoneal dialysate and a condensed and purified solution of a patient's own plasma-protein components contained in the collected dialysate without the risk of residual toxicity, as well as to preserve [the condensed and purified solution] in an aseptic state.

[Resolution] The condensed solution of plasma-protein components is maintained under a strongly acidic condition of pH 4-0, and is neutralized with alkali at the time of actual usage. Alternatively, said condensed solution is kept at a cool temperature within the temperature range of -80°C to 10°C and is then warmed up to body temperature when actually infusing [Lit., using the solution into the patient's body]. The inside of the collection/regeneration device is periodically disinfected with strongly acidic electrolysis water. The filter and the semi-permeable membrane condenser provided in said device, as well as the aseptic filter at the upper-stream area of an infusion catheter, are filled with an antibacterial agent. Microwaves are irradiated when disconnecting and reconnecting the terminal areas of the device and catheter in order to replace the catheter. Additionally, the above-mentioned means can be applied in a combination of two or more.



[Claims]

[Claim 1]
A method of sterilizing and preserving peritoneal dialysate in a dialysate-regeneration process, which includes steps such as:

Collecting the peritoneal dialysate flushed out of the patient's [Lit., human] body through a drainage catheter,

Removing harmful metabolites from it, and then condensing, and

Purifying [the collected dialysate] in order to reuse the plasma-protein component contained in the collected dialysate as a colloidal-osmotic pressure agent;

Wherein a strong acid is added to said condensed and purified solution, [the compound solution] is preserved under a strongly acidic condition of pH 4~0, alkali is added therein and the pH level is adjusted to pH 6~8 when preparing a regenerated dialysate [for an actual use] using said solution being preserved.

[Claim 2]
A method of sterilizing and preserving peritoneal dialysate that is characterized by preserving the condensed and purified solution of Claim 1 by cooling it down to the temperature range of -80°C to 10°C and then warming [it] up to the temperature range of 35°C to 40°C when infusing [Lit., using] the regenerated dialysate (which is prepared using said condensed and purified solution) into the patient's [Lit., human] body.

[Claim 3]
A sterilization and disinfection method of a dialysate collection/regeneration device wherein the principal parts are comprised of:

Peritoneum catheters for infusing and flushing out the dialysate from a [patient's] abdominal cavity (2, 19);

A means to filter the dialysate collected from the abdominal cavity (6);

A condensing/purifying means to remove harmful metabolites in a collected dialysate and purify the plasma-protein component (7, 8, 9, 10, 11);

A means of sterilizing and preserving the condensed and purified solution as needed (12, 13); and

A means to prepare a regenerated dialysate by adding useful components to the condensed and purified solution (14, 15, 16).

Wherein each of the above-mentioned means except said sterilization and preservation means (12, 13) and the wetted parts of the dialysate path connected to said [means] are rinsed with alkaline water, (after said rinsing process) immersed in the strongly acidic electrolyzed water produced through an electrolysis of sodium chloride at the anodal side for at least three minutes, and then rinsed with sterile water.

[Claim 4]
A sterilization and disinfection method of Claim 3 using strongly acidic electrolyzed water with pH 3~0 (the pH generated through an electrolysis of sodium chloride at the anodal side), redox potential of at least 900mV, and available chlorine concentration of at least 0.8 ppm.

[Claim 5]
A method of sterilization and disinfection wherein any one or more of the dialysate filtration means (6), the condensing means (9) and the aseptic filter (23) provided at the upper-stream area of the infusion catheter in the dialysate collection/regeneration device of Claim 3, are filled with an antibacterial agent.

[Claim 6]
A sterilization and disinfection method of Claim 5 wherein silver particulates or an antibiotic is supplied as the antibacterial agent.

[Claim 7]
A sterilization and disinfection method wherein high-frequency electromagnetic waves are irradiated for at least 10 seconds on the coupling parts (3a-3n) of the dialysate path and the flow path of additive solutions within the dialysate collection/regeneration device of Claim 3.

[Claim 8]
A collection/regeneration device of peritoneal dialysate, as well as a sterilization and disinfection method of the condensed and purified dialysate comprised in combination of any two or more of the methods of claims 1, 2, 3, 5 and 7.

[Detailed Description of the Invention]

[0001]

[Technological Field of the Invention]

The present invention includes a method used for peritoneal dialysis (one of the treatment methods of renal failure), which sterilizes and prevents the growth of bacteria and viruses that might infiltrate from the exterior into a dialysate collection/regeneration device and a condensed and purified dialysate while said dialysate is being preserved. Additionally, said dialysate collection/regeneration device collects the dialysate flushed from the system [Lit., human body], and then condenses and purifies the plasma-protein component exuded from the patient's body [Lit., inside the body] contained in said eccrisis dialysis drainage, so as to reuse [it] by adding [it] into a dialysate as a colloidal-osmotic pressure agent.

[0002]

[Conventional Technology]

Conventionally, formalins were the primary means for the disinfection/sterilization method of an artificial kidney or a dialyzer. However, an issue of residual toxicity arose in regard to such means. Accordingly, sodium-hypochlorite solutions have been used [for that purpose]. Nevertheless, this disinfectant cannot be applied to the sterilization of viruses and bacteria that have intermingled with the plasma-protein component that will be infused back into the [patient's] abdominal cavity as a regenerated dialysate.

[0003]

Moreover, in a manner differing from the dialyzers used in hospitals or dialysis treatment centers, those regeneration devices installed in a patient's residence (as shown in Figure 1) are not appropriate for disinfection with sodium hypochlorite, which requires a large volume of sterile water for rinsing after the disinfection.

[0004]

Additionally, the patent publication of JP 06-104120, for example, includes a description of providing a submicron filter to prevent bacteria and viruses that infiltrate from the terminal area (3n) of the catheter used for infusing the regenerated dialysate into the abdominal cavity. However, [with this method] an alternative disinfection method must be provided separately for sterilizing bacteria that grow on the aseptic filter (23) itself. Therefore, it is still constrained by the same restrictive conditions as the above-mentioned [method] concerning residue from the disinfectant and the water used for rinsing.

[0005]

Moreover, the sterilization of each terminal area (3a-3n) of a regeneration device cannot be adequately achieved through the ultraviolet irradiation method currently employed in the

conventional technology when it comes to the sterilization of parts for which ultraviolet rays cannot provide sufficient penetration. Furthermore, it is necessary to facilitate an environment that allows sufficient sterilization when disengaging the terminal areas.

[0006]

[Problems to Be Resolved by the Invention]

The plasma-protein components serving as the subject of sterilization and preservation, according to the present invention, consist of albumin, globulin, etc. [These plasma-protein components] can be reused and infused back into the patient's abdominal cavity with a dialysate, while a part of the component can enter the intracorporeal [system] through absorption via lymph vessels. Accordingly, there is a risk of harmful effects if the sterilant or disinfectant remain therein. Therefore, there has been a demand for a method of sterilization and disinfection that poses no risk of disinfectant residue.

[0007]

When attempting to sterilize a condensed, purified solution of a plasma-protein component by heating, sufficient sterilization cannot be performed unless it is heated to a much higher temperature than the denaturation point of protein (60℃ - 80℃). [Accordingly,] there has been a demand for a method of sterilization and preservation that does not denature protein.

[0008]

Meanwhile, for a method of periodic sterilization and disinfection of a dialysate path and the flow path of additive solutions within a regeneration device, a method similar to the conventional disinfection method of dialyzers can be applied. Nevertheless, a method of disinfection and sterilization should desirably have less residual toxicity and require less rinsing water for the rinsing process after the disinfection process.

[0009]

Additionally, concerning the sterilization of each terminal area that connects the dialysate path and the flow path of additive solutions within a regeneration device (3b-3m) and the terminal area (3a) of a drainage catheter or the terminal area (3n) of a clysis catheter, there has been a demand for a disinfection method that is also compatible with the latest terminal-area materials, such as ceramics, as well as [a type that] can provide [Lit., perform] sufficient sterilization [more effectively] than an ultraviolet-irradiation method.

[0010]

[Means for Resolving the Problems]

An environmental condition that can hinder the survival and growth of bacteria intermingled

with the plasma-protein component typically includes factors such as, for example, temperature (above 120°C, or below -20°C), concentration of salt in a highly concentrated mineral-salt solution, dry condition and pH (below 4, or above 12). Given the above, [a study was conducted to] examine the conditions that could preserve/store plasma-protein components within the range of reversible reaction or reversible secondary-structure transformation, wherein the dry-treatment that pertains to the handling of powder was excluded [Lit., avoided] from the process, in order to [achieve] the goal of managing the process through a fully automated system. As a result, the present invention according to Claim 1 adds a strong acid to a purified dialysate containing a condensed plasma-protein component, and preserves [the solution] at below pH 4 (preferably at pH 0~3 [Lit., 3~0]), neutralizes [it] with alkali before reusing [it] by adding this [solution] to a dialysate again, and then reusing [it] by adjusting the pH to 6~8 and restoring the plasma-protein component to its original condition.

[0011]

Although a highly concentrated salt solution can prevent bacterial growth, there is also an unfavorable action that leads to the deposition of albumin etc. Therefore, such solution [Lit., this] is not actively used in the present invention.

[0012]

Albumin (which is the base component of a plasma-protein component) is dissolved into a eccrisis dialysate through bonding with urea, etc. [With this structure,] urea is isolated by strong chloride, resulting in an acid expansion, and then the proteinic secondary structure is transformed from the F type to the E type at pH 3.6 to 2.8. Therefore, sterilization is effectively performed within the conditional range wherein the protein transforms reversibly.

[0013]

Furthermore, to remove harmful metabolites and prevent the growth of bacteria while the dialysate (which contains a condensed, refined plasma-protein component) is being stored, the present invention (according to Claim 2) cools down the plasma-protein component to a low temperature (i.e., above -80°C but below 10°C). And then, [right] before infusing [it] into [the patient's] abdominal cavity, the present invention (according to Claim 2) warms [it] up to body temperature and infuses [the warmed-up dialysate into the patient's abdominal cavity].

[0014]

According to Claim 3, in order to periodically sterilize and disinfect the inside of a regeneration device, the present invention uses strongly acidic electrolyzed water (an anodal product of an electrolyzed sodium chloride water) that is far more potent and with

much lower concentration compared with conventional highly concentrated sodium-hypochlorite solution.

[0015]

Nevertheless, because the effect of the above-mentioned electrolyzed water diminishes under a coexisting condition with a reducing substance, it becomes necessary to remove the organic substances in the dialysate path. Therefore, [the inside of the regeneration device] must be rinsed with alkaline water beforehand and, after rinsing, disinfected using strongly acidic electrolyzed water.

[0016]

As described in Claim 4, strongly acidic electrolyzed water (produced at the anodal side through an electrolysis of sodium chloride) with pH 0~3 [Lit., 3~0], redox potential of at least 900mV, and available chlorine concentration of at least 0.8 ppm, is preferable as the electrolyzed water [according to the present invention].

[0017]

[The components in a regeneration device] such as a pre-filter (6), semi-permeable membrane condenser (9) and the aseptic filter (23) of a clysis catheter contain the conditions for easy bacterial growth, since each of them has cells, fibrins and proteins, etc., adhering therein. However, a large quantity of electrolyzed water is required when sterilizing these parts using the above-mentioned strongly acidic electrolyzed water, since it is consumed by the large volume of organic substances that adhere within. Consequently, as a new means to prevent bacterial growth, the present invention (according to Claim 5) fills an antibacterial agent into the pre-filter part (6) (a dialysate filtration means), the semi-permeable membrane condenser (9) (a dialysate condensation means) and the aseptic filter (23) provided in the upper-stream side of the clysis catheter in advance, and thereby sterilizes the viruses and bacteria that adhere to and survive on the filters.

[0018]

As described in Claim 6, the antibacterial agent used [in the present invention] is [a type] in which silver particulates or antibiotics are immobilized through an ordinary means.

[0019]

As a method of preventing contamination during the process of disconnecting and reconnecting the terminals of the additive solution feeders [Lit., for feeding the additive solutions] and the terminals of the dialysate path (3a-3n) by manipulating from outside the regeneration device, the present invention according to Claim 7 uses irradiation of radio-frequency electromagnetic waves (microwaves), by which the above-mentioned terminal areas (3a-3n) can be instantaneously heated to a high temperature. For said irradiation it is necessary to use microwaves at frequencies from 500 to 8000 MHz for a duration of at least 10 seconds.

[0020]
To further and thoroughly achieve the purpose/objective of the present invention, as described in Claim 8, the overall sterilization and disinfection effect can be improved without any physiological hindrance/interference if any two or more of the above-mentioned means are applied in combination.

[0021]
[Examples]
Strong acid (preferably chloride) is added to the condensed, purified solution of a plasma-protein component so as to preserve [the solution] after adjusting the pH to below 4, preferably in the range of pH0 to 3.
[0022]
The plasma-protein component stored in a strongly acidic condition is used after being neutralized with alkali to the pH range of pH 6 to 8, preferably in the range of pH 7.2 to 7.6. A preferable alkali [according to the present invention] is a mixture of sodium hydroxide or sodium carbonate with sodium bicarbonate.
[0023]
An electrolyzer (4) that electrolyzes a dilute sodium-chloride solution and produces a so-called strongly acidic electrolyzed water (which contains sodium hydroxide solution at the cathode and hypochlorous-acid ion and chlorine ion, etc., at the anodal side) is incorporated into the regeneration device. The above-mentioned strongly oxidizing aqueous solution is supplied as a disinfectant and rinse water when needed.
[0024]
Bacteria cannot survive in conditions of pH under 3.0, redox potential above 900mV and available chlorine above 0.8 ppm. Accordingly, the inside of the regeneration device is sterilized and disinfected by immersing the wetted part of said device in the above-mentioned strongly acidic electrolyzed water and maintaining said device in the state of fulfilling these conditions for a given duration of time, preferably for 5 minutes.
[0025]
The bactericidal effect of the strongly acidic electrolyzed water is demonstrated to the maximum extent when the organic substances adhering in the dialysate path are removed by flushing alkaline water (produced at the cathode of the above-mentioned electrolyzer (4) as a byproduct) into said device prior to the disinfection process.
[0026]
To prevent the growth of bacteria that would otherwise adhere to the components provided in the device such as pre-filter (6), semi-permeable membrane condenser (9) and the

aseptic filter (23) of a clysis catheter, said effect can be enhanced by filling up an antibacterial agent in these parts in advance. As the antibacterial agent, antibiotics, for example, vancomycin against gram-positive bacteria, ceftazidime or aminoglycoside against gram-negative bacteria, and against fungi, agents with flucytosine or fluconazole immobilized using an ordinary method, as well as silver particulates, can be used.

[0027]

In all the above cases the aseptic filter connected to the inlet of the clysis catheter is inserted into the [patient's] abdominal cavity immediately after the dialysate passes through the filter. Therefore, the use of another sterilization method is restricted. An antibiotic that can be administered into the patient's abdominal cavity, or alternatively silver, is particularly suitable for this condition.

[0028]

In the event of disconnecting and changing the terminal areas (3a, 3n) connected to the terminal areas (3b~3m) and the peritoneum catheter (2, 19) in the regeneration device, these terminal areas and the new coupling parts are simultaneously irradiated with microwaves at a frequency from 500 to 8000 MHz for at least 10 seconds (preferably 30 seconds) under a high-temperature and high-pressure atmosphere within a pressure-resistant sealed/hermetic container. Subsequently, the high-pressure steam generated therein is released from the sealed container. The old [Lit., existing] terminals are disconnected by manipulating [the container] from the outside so that the inside of the container will not be exposed to the ambient air. After irradiating [microwaves] for at least 10 seconds or longer as needed, new coupling parts are connected to the terminals. The above-mentioned microwaves are irradiated again for at least 10 seconds, preferably for approximately 30 seconds.

[0029]

An example of devices that can perform the above-mentioned replacement procedure includes the ones whose sealed/hermetic container has a pressure-resistance level of at least 1.5 Pb, and which is supplementary provided with an apparatus for extraction and interposition, or an apparatus associated with an operation such as a screw rotation that allows to disconnect an old [Lit., existing] terminal connection and connect a new coupling part through the external manipulation of the container. Such a device for replacing the terminal connections includes, for example, "UV Flush" by Baxter Inc., or similar product.

[0030]

Although the above-mentioned microwaves can be applied with a high frequency from 500 to 8000 MHz, approximately 2450MHz is preferable in all the above cases due to the extremely high exothermic and bactericidal effects.

[0031]

[Effect of the Invention]

The present invention makes it possible to perform the safe, sanitary regeneration of the plasma-protein component without causing pathogenic bacterial infections, a recycling [of the plasma-protein component] as a colloidal-osmotic pressure agent, and the most physiologically sensible ultrafiltration, which is easy on the peritoneum. Therefore, it is no longer necessary to use the high concentration of glucose dialysate that has conventionally been used. Accordingly, it can resolve issues associated with the side effects resulting from the glucose, such as (1) progression of diabetes symptoms, (2) hyperlipidemia and/or progression of arteriosclerosis, (3) onsets of peritonitis due to frequent occurrences of pathogenic-bacterial infections and (4) functio laesa (function loss) of the peritoneal dialysis.

[0032]

Furthermore, the method provided by the present invention as the method of sterilizing and preserving the plasma-protein component contained in the condensed, purified dialysate is also effective in implementing economical peritoneal dialysis because it can facilitate safe and long-term preservation [of the solution] in a ready-to-use condition, thereby eliminating a loss of the patient's own valuable plasma-protein components due to degeneration or decay.

[0033]

[Brief Explanation of the Drawings]

[Figure 1] is a block diagram illustrating the entire structure of a device for implementing the method of the present invention.

[0034]

[Figure 2] is a sectional view of an aseptic filter illustrating the method of the present invention according to Claim 5.

[0035]

[Figure 3] is a sectional view of a pre-filter illustrating the method of the present invention according to Claim 5.

[0036]

[Figure 4] is a sectional view of a semi-permeable membrane condenser illustrating the method of the present invention according to Claim 5.

[0037]

[Description of Notations]

1 ..... Abdominal cavity

2 ..... Drainage catheter

3a~3n .. Connectors (coupling part)

4 ..... Strongly acidic electrolyzed-water generator

5 ..... Pump

6 ..... Pre-filter

7 ..... Collected dialysate reservoir

8 ..... Diluent feeder

9 ..... Condenser

10 ..... Concentrated-solution reservoir

11 ..... Rinsing-water feeder

12 ..... Chloride feeder

13 ..... Concentrated/purified-solution reservoir

14 ..... Alkali feeder

15 ..... Electrolyte feeder

16 ..... Regenerated-dialysate reservoir

17 ..... Fresh dialysate bag

18 ..... Warmer

19 ..... Clysis catheter

20 ..... Measurement instrument

21 ..... Pre-filter antibacterial-agent filling part

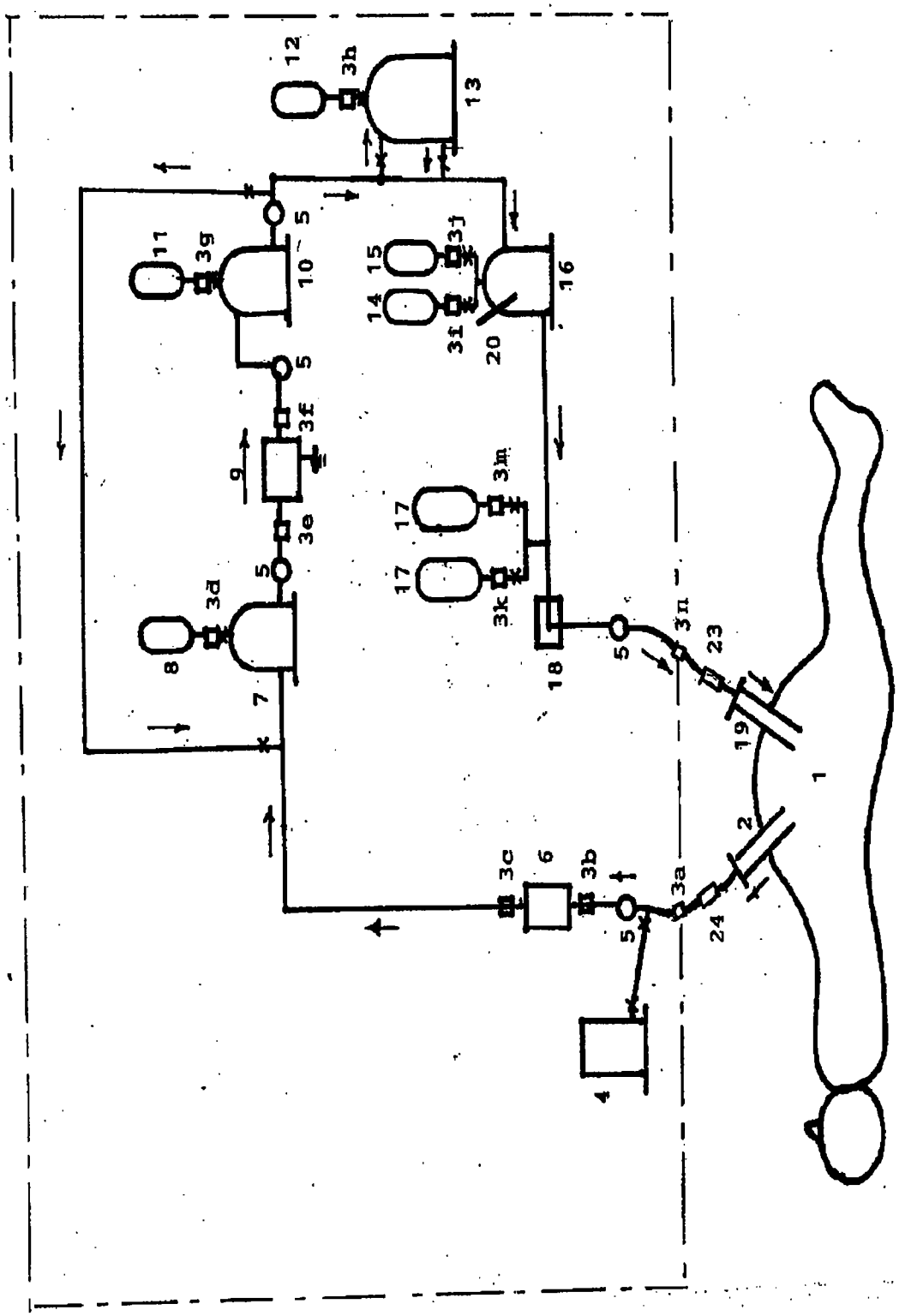
22 ..... Condenser antibacterial-agent filling part

23 ..... Aseptic filter

24 ..... Check valve

25 ..... Aseptic filter antibacterial-agent filling part

[Figure 1]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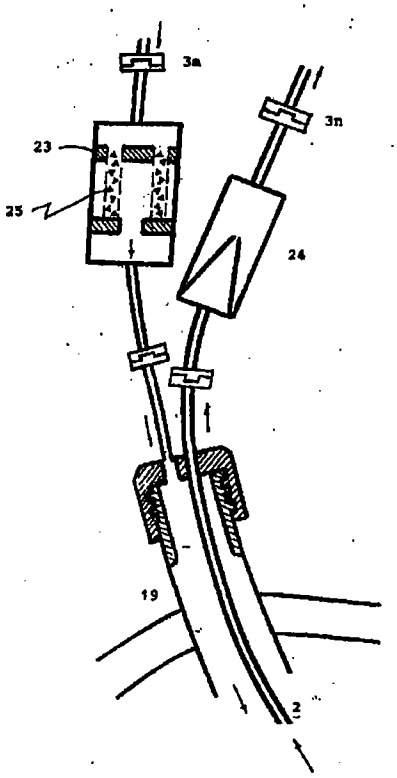
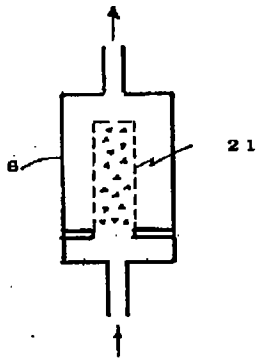
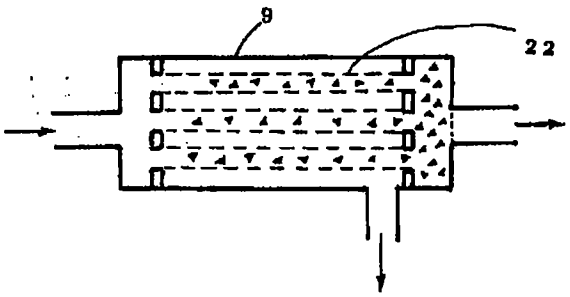
[Figure 2]



[Figure 3]



[Figure 4]



Cont'd from the cover page.

(51) Int. Cl.[6] ID Symbol
A61L 2/16

2/18

F I
A61L 2/16 A
Z
2/18

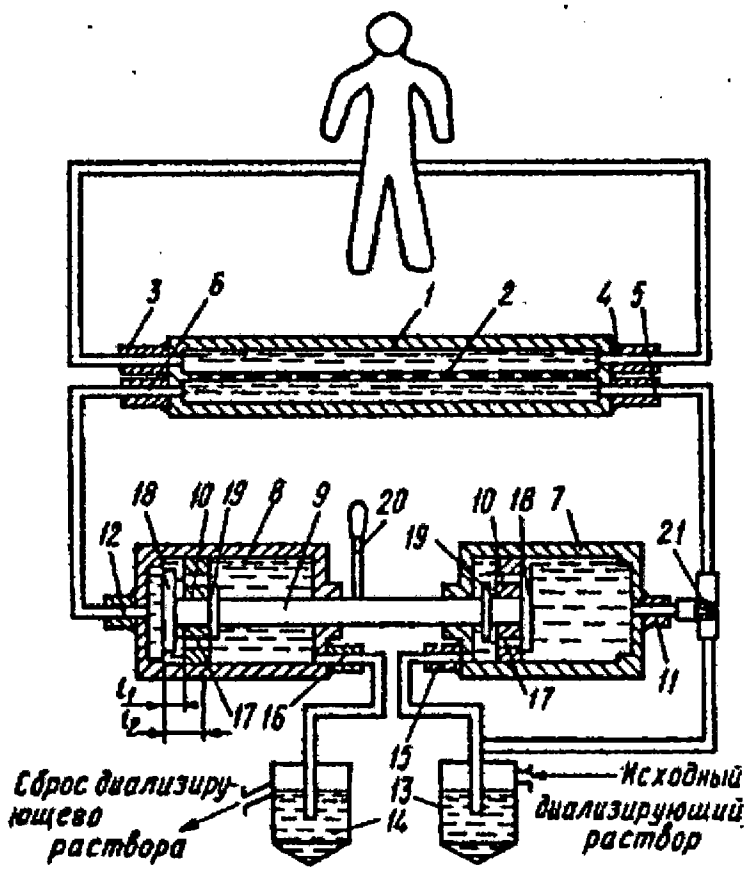
Union of Soviet
Socialist Republics
[state emblem]

USSR State Committee for
Inventions and Innovations

DESCRIPTION OF THE INVENTION
APPLICATION FOR AUTHOR'S CERTIFICATE

(19) SU (11) 1344362 A1
(51) 4 A 61 M 1/16, B 01 S 13/00

(21) 3759334/28-14
(22) 28.06.84
(46) 15.10.87 Bulletin No 38
(75) F. I. Mikheev, B.G. Zakharov, E. G. Patrushev, and V. K. Gusev
(53) 615.475 (088.8)
(56) US Patent No. 4208289,
cl. B 01 D 13/00, published: 1980
US Patent No. 4178240,
cl. B 01 D 31/00, published: 1979
(54) APPARATUS FOR DIALYSIS
(57) The invention deals with the field of medicine and may be utilized for cleansing biological fluids of toxic ingredients. The aim of the invention is to enhance the performance of the apparatus. The upper part of the casing 1 is connected, via connecting pipes 3 and 4, with the source of biological fluid. The lower part of casing 1, cylinders 7 and 8, and vessels 13 and 14 are filled with dialyzing solution that circulates, in the course of dialysis, along the membrane 2 performing vibratory movements. Dialysis conditions are improved by means of an impulse action of pulsating flow on the para-membrane layer. Claim 1 of the invention, Figure 1.



Flushing
of dialyzing solution

Source
dialyzing solution

The invention deals with the field of medical technology, in particular with devices for cleansing biological fluids of toxic ingredients, for example blood, in the process of hemodialysis and may also be utilized in other areas of technology, such as chemical technology.

The aim of the invention is to enhance the performance of the apparatus and decrease the consumption of dialyzing solution by means of vibratory movements of the dialyzing solution along the membrane.

The drawing represents the main scheme of the apparatus for dialysis.

The apparatus contains casing 1 with horizontal semi-permeable membrane 2, inflow pipes 3 and outflow pipes 4 which provide inflow and outflow [respectively] of a biological fluid, for example blood, from one side of membrane 2, and inflow pipes 5 and outflow pipes 6 which provide inflow and outflow [respectively] of a dialyzing solution from the other side of membrane 2, and identical cylinders 7 and 8 of the source dialyzing solution. Both cylinders 7 and 8 are equipped with one identical piston 10, the pistons being located on the main rod 9. Pipe-lines connect one side on cylinder 7 provided for the dialyzing solution, the said side having connecting pipe 11, with inflow pipe 5, and at the opposite side of the second cylinder 8, this side having connecting pipe 12, with outflow pipe 6. Moreover, the apparatus is additionally equipped with vessel 13 for source dialyzing solution and the vessel 14 for waste dialyzing solution, which vessels are connected via pipe-lines with the sides of cylinders 7 and 8, respectively, positioned opposite to the sides connected with casing 1 and having connecting pipes 15 and 16, respectively. Pistons 10, fixed on rod 9 with the possibility of relocation, have through openings 17; at the ends on rod 9 there are plates 18 that provide cover of the openings 17, while at the other side of the pistons 10 there are limiting plates 19 located in a way so that plates 18 do not reach the walls of cylinders 7 and 8 at the end portions of rod 9. Cylinders 7 and 8 are located at a distance from one another, there is also a handle 20 positioned on rod 9 between cylinders 7 and 8, which handle is necessary for setting rod 9 into

movement. Pipe-line connecting pipes 5 and 11 may be additionally connected, via T-valve 21, with vessel 13 provided for source dialyzing solution, which allows maintaining the supply of dialyzing solution for the apparatus and the simultaneous elimination of the same volume of waste dialyzing solution from vessel 14. The apparatus for dialysis operates in the following way.

The upper part of casing 1 is connected, via connecting pipes 3 and 4, with the source of biological fluid, for example, a patient. The lower part of casing 1, cylinders 7 and 8, and vessels 13 and 14 are filled with dialyzing solution that circulates, in the course of dialysis, along the membrane 2 performing vibratory movements.

The circulation of dialyzing solution is achieved in the following way.

Rod 9 is moved from the initial position, with handle 20, towards connecting pipe 12, whereas piston 10 in cylinder 8 comes into contact with the limiting plate 19, but does not come to contact with plate 18 and the openings 17 are not covered. In this phase piston 10 in cylinder 7 performs the opposite, i.e. it comes into contact with plate 18, but does not come to contact with the limiting plate 19 and the openings 17 in piston are covered. Dialyzing solution flows towards cylinder 7 by means of suction power created in the cylinder with piston 10. Piston 10 in cylinder 8 moves at a distance l_1, which is followed by the movement of rod in the opposite direction at a distance l_2 corresponding to the movement of piston 10 in cylinder 8 and being larger than l_1. At that time openings 17 of piston 10 in cylinder 8 are covered with plate 18, while openings 17 of piston 10 in cylinder 7 are not covered with plate 18. In this way the dialyzing solution flows from vessel 13, through casing 1, towards cylinder 8, while the waste dialyzing solution from cylinder 8 outflows into vessel 14. Due to $l_2 > l_1$, rod 9 moves to the extreme right position where the limiting plate 19 in cylinder 8 comes into contact with the cylinder's wall having the connecting pipe 16, while plate 18 in cylinder 7 does not reach the cylinder's wall having the connecting pipe 11. Next, the process is repeated, without pause in the movement of rod 9, into the opposite direction, in which process the connecting pipes 11 and 12 do not come into contact with plates 18, neither do the connecting pipes 15 and 16 come into contact with pistons 10 at any phase of the apparatus's operation.

In the course of the said operation of the apparatus the dialyzing solution performs vibrating movements along membrane at its reverse introduction into casing 1. This allows improving the conditions of dialysis by means of an impulse action of pulsating flow on the para-membrane layer that determines the speed of mass transfer resulting in enhanced efficacy of this arrangement. Due to prolonged circulation of the dialyzing solution, a higher final concentration, in the dialyzing solution, of the substance to be eliminated is obtained, and therefore the necessary consumption of dialyzing solution can be decreased.

Formula of the invention

Claim 1. Apparatus for dialysis containing a casing with horizontal semi-permeable membrane, pipes providing outflow and inflow of a biological fluid at one side of the membrane, and pipes providing outflow and inflow of a dialyzing solution at one other of the membrane, identical cylinders for source and waste dialyzing solution, which both cylinders each have an identical piston positioned on the main rod, pipe-lines connecting one side of the cylinder for source dialyzing solution with inflow pipes, and connecting the opposite side of the second cylinder with outflow pipes provided for the outflow of dialyzing solution, the characteristic feature of the apparatus being that, in order to enhance the performance and decrease the consumption of dialyzing solution by means of vibrating movement of dialyzing solution along membrane, the apparatus is additionally equipped with vessels for the source and waste dialyzing solution, which vessels are connected via pipe-lines with the sides of the cylinders provided for the source and waste dialyzing solution, respectively, and positioned opposite to the sides connected with the casing, wherein the pistons are fixed on a rod with the possibility of relocation and have through openings, wherein at the ends on the rod there are plates provide cover of the openings, while at the other side of the pistons there are limiting plates located in a way so that the plates at the ends of the rod in its extreme position do not reach the walls of the cylinders, the cylinders being positioned at a distance from one another, moreover, there is a handle positioned on the rod between the cylinders.

Claim 2. The apparatus of claim 1, its characteristic feature being that a pipe-line connecting cylinder provided for source dialyzing solution with casing is additionally connected, via T-valve, with a vessel provided for the source dialyzing solution.

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Editor M. Andrushenko | Tech. Editor L. Oleynik | Proofreader M. Demchik

Order 4871/6 | Circulation 1594 | Signed

CNIIPI of State Committee for Inventions and Innovations USSR
113035, Moscow, Ж-35, 4/5 Raushskaja nab.

Branch of Publishing house "Proyekt", 4, Proektnaja st., Uzhgorod

METHOD FOR RECOVERING AND REGENERATING PERITONEAL DIALYZATE, APPARATUS THEREFOR, AND ATTACHMENTS THEREOF

Patent number: WO9747337
Publication date: 1997-12-18
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Classification:
- international: ***A61M1/28;*** *A61M1/16;* **A61M1/28;** A61M1/16; (IPC1-7): A61M1/28
- european: A61M1/28; A61M1/28C
Application number: WO1997JP01950 19970609
Priority number(s): JP19960150930 19960612

Also published as:
EP0928615 (A1)
JP9327511 (A)
EP0928615 (A4)

Cited documents:
JP8337590
JP4327857

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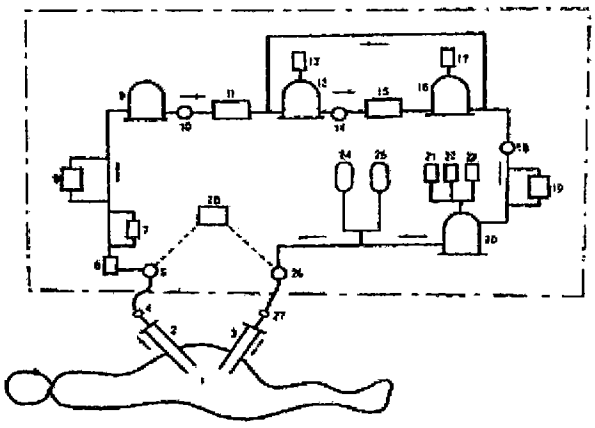
Abstract of **WO9747337**

A method for regenerating a peritoneal dialyzate employed in peritoneal dialysis for treating renal insufficiency and recovered therefrom and an apparatus and its attachments thereof to be used therefor. To circulate and reuse a peritoneal dialyzate with the use of the plasma proteins of a patient himself as a colloidal osmotic agent, the discharged peritoneal dialyzate is sanitarily recovered and uremigenic factors are eliminated therefrom without denaturing the plasma proteins. At the same time, its osmotic pressure is elevated and the dialyzate is regenerated as a physiologically efficacious and safe peritoneal dialyzate in the following manner. By using a semipermeable membrane having an appropriate inhibitory fractional molecular weight, the recovered peritoneal dialyzate is concentrated to such an extent that the plasma proteins contained therein are not denatured and then diluted with a physiologically efficacious electrolyte solution. By repeating these procedures, uremigenic factors are filtered off and the excessive moisture is also removed therefrom to thereby elevate the osmotic pressure of the dialyzate. If needed, useful components such as electrolytes or amino acids are added.



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 928 615 A1

(12) **EUROPEAN PATENT APPLICATION**
published in accordance with Art. 158(3) EPC

(43) Date of publication:
14.07.1999 Bulletin 1999/28

(21) Application number: **97924350.8**

(22) Date of filing: **09.06.1997**

(51) Int. Cl.[6]: **A61M 1/28**

(86) International application number:
PCT/JP97/01950

(87) International publication number:
WO 97/47337 (18.12.1997 Gazette 1997/54)

(84) Designated Contracting States:
BE DE FR GB IT NL SE

(30) Priority: **12.06.1996 JP 15093096**

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(54) METHOD FOR RECOVERING AND REGENERATING PERITONEAL DIALYZATE, APPARATUS THEREFOR, AND ATTACHMENTS THEREOF

(57) The present invention is a recovery and regeneration process of peritoneal dialysate for chronicle renal failure patient and an apparatus therefor and an attachment thereof.
For recycling the patient's plasma protein as osmotic agent in peritoneal dialysis liquor, the effluent is recovered and uremic toxin is removed without denaturing the plasma protein under sterile condition and concentrated to the consistency to create hyper-osmolality so as to regenerate the efficient and physiologically safe dialysate by the following way ;
The recovered liquor is concentrated with semi-permeable membrane to the consistency not so high as to be denatured and thence diluted with sterile water or physiological electrolyte solution repeatedly a few times, so that small molecule uremic toxin and excess liquor is removed to raise the osmolality. If needed, electrolyte, amino acid or other useful solute is added for obtaining hyper-osmolality.
The invention also provides the apparatus and the attachments for the process.

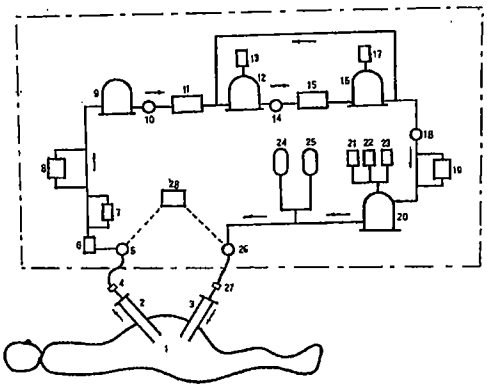


Figure 1

EP 0 928 615 A1

Description

FIELD OF THE INVENTION

[0001] The present invention relates to the recovery and regeneration process of peritoneal dialysate that is used for dialysis therapy of renal failure, from which uremic toxin is removed, if needed, any useful components are supplemented for its reuse and its apparatus and attachments for the process

BACKGROUND OF THE INVENTION

[0002] As the therapy for chronic renal failure disease, hemodialysis has been widely applied in the world and enteral uremic toxin absorber is used before starting dialysis.. Additionally continuous ambulatory peritoneal dialysis has been also applied and recognized to have many advantages over hemo-dialysis as it removes uremic toxin continuously through the patient's peritoneum like living kidney does, compared with hemodialysis which uses artificial semipermeable membrane, and it allows the patient receive the therapy at patient home so that he has longer free time for social activity. However peritoneal dialysis has a few problems to be improved as follows;

[0003] In peritoneal dialysis, the dialysate is infused into the patient peritoneal cavity through the implanted catheter and after a few hours dwelling or recirculating, it is drained out. This procedure is repeated a few times a day. The dialysate is made of electrolyte solution. The chronical renal failure patient is incapable to exclude uremic toxin into urine. Consequently in peritoneal dialysis therapy, uremic toxin such as urea, creatinine and uric acid are diffused out from blood vessel through peritoneum into dialysate in peritoneal cavity.

[0004] Also excess liquid must be excluded from the body like kidney does in urine. In hemo-dialysis, extracoporeal blood circulation line is kept at higher pressure against dialysate circulation line, so excess liquor in blood is squeezed out through the dialyzer membrane.

[0005] In peritoneal dialysis, such static pressure difference may not be created between blood and dialysate. Consequently hyperosmotic solution is used as dialysate in which excess liquid in the patient body is ultrafiltered through peritoneum by osmotic pressure gradient. Hyperosmotic dialysate is prepared by dissolving oncotic agent such as glucose into electrolyte solution at significantly high consistency. However it is observed recently that after long term dialysis, CAPD patients suffer from severe adverse effect due to the intake of a large quantity of glucose that is added as oncotic agent through peritoneum from the dialysate every day; such as, obesity, hyperlipemia(high triglyceride consistency in serum), arterial vessel sclerosis and worsened diabetes

[0006] In order to avoid such adverse effect, various alternative oncotic agents to replace glucose have been attempted, such as oligosaccharides, hydrolyzed polysaccharides, amino acid, or hydrolyzed protein.
However every substitute has been reported to cause new problems; disturbance of metabolism, increase in maltose consistence in serum with oligo- and polysaccharides, high cost with amino acid, caramel reaction with mixture of amino acid and sugar, allergy reaction with gelatin and hydrolyzed protein, etc, if these are used in large quantity every day..
Albumin has been recognized as most physiological osmotic agent, However a large quantity of albumin from plasma may not be collected for the source without problem in economy and anemia.

[0007] While ascite has been observed in some lever, pancreas and womb cancer patients and it contains protein in similar consistency to that in serum. For therapy of the disease, the ascite is withdrawn out of abdominal cavity, concentrated and re-infused into the patient venous vessel. In case it was returned to abdominal cavity instead of venous vessel, it was reported to improve edema. However these patients had no renal dysfunction disease, the ascites did not contain uremic toxin so that no attempt was made to remove the toxin.

[0008] The present invention aims at recovering albumin and other plasma protein from the peritoneal dialysis effluent ,removing uremic toxin ,concentrating it and reusing it as osmotic agent in place of glucose, thence resolving the physiological and clinical problems due to adverse effect of glucose that is used as oncotic agent. The key point is how to recover the said protein without denaturing out of the dialysis effluent, how to remove uremic toxin and how to accumulate it at high consistency under sterile conditions and how to reuse it.

[0009] The present invention also relates to the instrument and ancillaries for the process.

DESCRIPTION OF THE INVENTION

(Recovery and Regeneration of Peritoneal Dialysate)

[0010] The present invention relates to the process to repeat the unit procedure of concentrating the plasma protein without denaturing with semi-permeable membrane of appropriate cut-off point (maximum permeable molecular weight) and diluting the concentrate with physiologically efficacious liquor, so as to remove small molecular weight ure-

mic toxin out of the dialysis effluent, and to concentrate the high molecular solute to high colloidal osmolality thence to supplement electrolyte salt and any useful components for regenerating peritoneal dialysate.

(Recovery and Regenerating Apparatus)

[0011] The apparatus of the present invention is a recovery and regenerating Apparatus, which comprises a novel draining catheter, unit devices to concentrate and to dilute peritoneal dialysate, and a novel infusing as main components.

(Attachments)

[0012] The attachments of the present invention comprises catheter, of which the middle part to implant under the abdominal skin, is in shape of single smooth cylindrical tube in which the dialysate is lead for infusion alone and draining alone respectively for improving recirculation flow of the dialysate in peritoneal cavity. The outer part and inner part of the catheter is divided in two tubes. The draining tube end is connected with reverse flow-proof valve and the infusing tube end is connected with bacteria-proof filter.

(Semi-permeable Membrane)

[0013] In the present invention, semi-permeable membrane with appropriate cut-off point is used for uremic toxin removal. Here "cut-off point" indicates the maximum molecular weight (dalton) to pass through.

[0014] Main uremic toxin, such as, urea, creatinine and uric acid are small molecular weight substance, below 200 dalton, while albumin has approximately 68,00 dalton molecular weight.

[0015] So that the cut-off point of the semi-permeable membrane of the concentrating unit (11,15) may be selected between the above two values, preferably between 500 and 30,000 to minimize the loss of albumin.

[0016] If the effluent contains substantial quantity of middle molecule (500—5,000 dalton) uremic toxin, the appropriate cut-off point would be between 5,000 and 30,000.dalton.

[0017] In case the patient has amyloidosis symptom, amyloid, for example, beta 2-micro globulin, must be removed. As the substance has 11,000 dalton molecular weight, the cut-off point should be between 15,000 and 30,000 dalton.

(Concentrating)

[0018] In concentrating procedure with semi-permeable membrane, the removing coefficient is estimated by the following formula; where the concentrating ratio by volume is C;

$$100 \times (1 - 1/C) = r$$

[0019] According to the above formula, as C increases r increases.
However if C exceeds a certain level, the protein loses the solubility and deposits irreversibly. Therefore the upper limit ofC must be not so great to make the protein hard to resolve again.
The lower limit would be as low as 1.5 times (a)
Below this level, the efficiency would be too small

(Diluting)

[0020] The limit of diluting ratio would be as follows;

Lower limit is as low as 0.5 times (b). Below this level next concentrating ratio is restricted to be lower than this level, resulting in uremic toxin removal efficiency too low.
Upper limit is practically physical limit. If the diluting liquor volume exceed 1,000 liter, the regenerated liquor reservoir (20) may not be easily installed at the patient home

[0021] In order to reduce the residual quantity of uremic toxin as low as 1/10 or preferably 1/25 , the cycle of concentration/ dilution unit procedure must be repeated once or a few times more

[0022] Diluting liquor could be sterile conventional peritoneal dialysate. Typical dialysate composition is shown in Table 2.
Main electrolyte salt, for example, NaCl, $MgCl_2$, $CaCl_2$, can be mixed with lactate or bicarbonate. Instead of electrolyte solution, sterile or bacteria free pure water can be used in this invention.

[0023] After the repeated concentration and dilution a few times, the final concentrate is adjusted to preset consistency by addition of diluting liquor and/or concentrate for regeneration of dialysate within the volume not exceed that of the effluent

(Pre-filtration)

[0024] In the effluent, cell and fibrin that is deposited plasma components are contained so that this solid is to be removed with pre-filtration(6).

(Absorption)

[0025] Among the globulin fraction with molecular weight 100,000—1,500,000 dalton, auto-immune antibody, complement, and lipoprotein are contained in case of rheumatism, lupus erythematosus and myasthenia gravis . If this malignant solute becomes accumulated to a high level in the recycled dialysate, it may suppress this substance to diffuse out through peritoneum into abdominal cavity furthermore. This is not desirable and halves the advantage of CAPD therapy. In order to remove these accumulated malignant fractions, before the first concentration, semi-permeable membrane (7) with cut-off point 100,000—1,000,000 dalton can be used. Also absorption column(8) that is made of, for example, porous copolymer of methyl methacrylate /divinyl benzene, epoxy cellulose gel, aspartylphenylalanine methylester or copolymer of stylene/divinyl benzene can be used. (d)

(Protein Supplement)

[0026] Usually peritoneal dialysis is performed a few times a day with low concentration glucose containing dialysate in addition to one or two hyper-osmotic dialysate for ultrafiltration. Into these dialysate plasma protein is diffused out through peritoneum every time. In the invented process, the newly diffused out protein may compensate partly or completely the loss of plasma protein during regeneration and contributes to maintaining mass balance

[0027] However in case of the patient whose malignant globulin is to be removed, loss exceeds diffused protein. In that case, required osmolality can be obtained with amino acid, albumin or oligomer of hydrolyzed protein.

(Catheter and other attachments)

[0028] In the apparatus according to the present invention, which is illustrated in Figure 1, a new type of catheter is used which was illustrated in the preceding patent application by the same applicant as does this patent, or described in the claims 8 and 9 of this invention. The catheter consists of two tubes; i.e. infusing tube (3) and draining tube.(2) in Figure 1.

[0029] In place of the above two catheters, the invented instrument can be connected with new double lumen type of catheter directly or through reverse-proof valve(33), bacteria-proof filter (34) and pump (26) with soft polyvinyl chloride tube.

(Concentrating unit)

[0030] In the concentrating unit (11,15) of drained liquor, semi-permeable membrane in shape of hollow fiber or folded membrane plate is used in which the drained liquor is introduced under pressure. The concentrating unit membrane can be made of any synthetic polymer or animal organ membrane.

(Electrolyte liquor supply unit)

[0031] In the apparatus according to the present invention, the electrolyte liquor supply unit (13, 17) is connected to the concentrate reservoir (12, 16) or the exit of the concentrating unit (11, 15). The material for this unit is not restricted as far as it does not denature water or electrolyte.

Supply of electrolyte liquor can be made either gravity or pump. The electrolyte liquor supply unit can be soft bag made of polyvinylchloride with valve or any other material that does not denature the liquor. As described, a pair of concentrating unit (11) and the electrolyte supply unit (13) can be repeatedly connected in a series,(15, 17) if needed. Otherwise the drained liquor can be recycled through a pair of the concentrating unit and electrolyte supply unit by connecting the exit of the electrolyte supply unit with the entrance of the concentrating unit and re-circulating with pump. The final exit of the above unit is connected with the regenerated liquor reservoir (20) then the exit of the reservoir is connected with pump (26) and the infusing catheter (3) through soft polyvinyl chloride tube.

(Filtration)

[0032] As described in Claim6, before the first concentration (11) , solid suspension such as fibrin are removed with the pre-filter (6) of which the pore size is below 100 nanometer. If needed, a large molecule globulin is removed with the semi-permeable membrane filter (7) of which cut-off point is between 100,000 and 1,000,000 dalton

(Automation system)

[0033] The invention in Claim 8 is automation system, which comprises automated regeneration system of peritoneal dialysate (g) andAutomated dialysate infusing and draining system (f).

[0034] The system (f) has the function to drain the dialysate from the patient abdominal cavity , that is stored for a few hours , through the draining catheter then to infuse the regenerated dialysate through the infusing catheter by opening and closing the valves and switch on and off the pumps according to the preset program in the satellite computer (40) or the order from the host computer(41).

Such an instrument is called "autocycler". Hyper-osmotic dialysate that is regenerated in the invention can be used in daytime or at night.

[0035] After keeping the effluent in the reservoir (9), the system (g) has the function to regenerate the dialysate, i.e. concentration, dilution and consistency adjustment, automatically in daytime, when the patient leaves away from the instrument for daily life, from the effluent recovered at night by the controller(42) according to preset program in the satellite computer (40) or the order from the host computer (41)

(Catheter)

[0036] The new catheter that is illustrated in Figure 2 is used in place of two catheters(2 and 3) illustrated in Figure 1. The implanted part in human ventral lateral tunnel of the catheter is in shape of a single tube for reducing bacteria invasion along the tunnel. The catheter comprises a con-centric double lumen tube(29), of which one(37) leads the liquor drain alone, the other(38) infusion alone.

[0037] The former end is connected with reverse flow-proof valve(33), while the latter is connected with bacteria-proof filter(34) and male/female connection terminal.

[0038] The catheter illustrated in Figure 3 .is in the shape of a single cylindrical tube in the middle part(30) in which two semicircle lumens lead the dialysate flow inward alone(36) and outward alone (35) respectively. The inner part and outer part are in the shape of divided two tubes.

(Other attachments)

[0039] Attachments described in Claim 11 are the reverse flow-proof valve(33) connected with the draining catheter exit(37) end so that it prevents flow back in of the liquor that flow out of the body once and bacteria-proof filter(34) of which membrane cut-off point is below 50 nanometer, connected with the infusing catheter entrance(38) that prevent bacteria invasion These attachments are exchanged by nurse once every month or two when the patient visits hospital.

(Use of the regenerated dialysate and the conventional one)

[0040] For the first few weeks after the invented instrument is installed at the patient's home, peritoneal dialysis is performed with conventional dialysate that contain glucose as osmotic agent while plasma protein is recovered from the effluent and accumulated in the reservoir until the quantity of protein reach to the sufficient level to provide 2 to 8 liter of hyper-osmolar dialysate .of which plasma protein consistency is greater than that of plasma, 6 to 8 gram/deciliter. Then dialysis with the regenerated dialysate is started. After the start, the loss of protein through the regeneration process may be compensated with the new diffused out protein approximately 9 g/liter from the patient body through peritoneum, except in case of specific complication, and maintain mass balance with help of small quantity of amino acid addition. .

(Conventional peritoneal dialysis with glucose containing dialysate)

[0041] Table 1 indicates dialysate composition, osmolality, ultrafiltration volume after dwelling in peritoneal cavity and energy intake based on glucose absorption through peritoneum from dialysate for each glucose content that is added as oncotic agent in dialysate at each osmotic pressure level

Typical example of usage per day is;

One bag of 4,25% dextrose (one molecule hydrate glucose)
and three bags of 1.5% dextrose or
two bags of 2.5% dextrose and two bags of 1.5% dextrose

With this prescription, 1 to 2 liter of ultrafiltration is gained, which is almost equivalent to healthy person's urine volume per day.
When the regenerated dialysate by the present invention is used, conventional 1.5-% glucose containing dialysate can be used. The regenerated hyper-osmolar dialysate take place of conventional 4.25% or 2.5% glucose dialysate.

Table 1

Dextrose Conc. %	Osmolality mOsm/l	Ultrafiltration Volume ml in 3 hours	Energy Intake kcal / 2 liter
1.5	346	150	80
2.5	396	320	140
4.25	485	900	280

BRIEF DESCRIPTION OF DRAWINGS

[0042]

Figure 1 Peritoneal Dialysate Regeneration System
Figure 2 Catheter of the Present Invention
Figure 3 Another Catheter
Figure 4 Computerized Regeneration System

Mark Number

[0043]

1-------- Abdominal Cavity
2-------- Draining Catheter
3-------- Infusing Catheter
4-------- Connector
5-------- Pump
6------- Pre-filter
7------- Filter
8------- Absorption Unit (1)
9------- Effluent Reservoir
10------ Pump
11------ Concentrating Unit (1)
12------- Concentrate Reservoir
13------- Electrolyte Liquor Supply Unit (1)
14------- Pump
15------- Concentrating Unit (2)
16------- Concentrate Reservoir (2)
17------- Electrolyte Liquor Supply Unit (2)
18------- Pump
19------- Absorption Unit (2)
20------- Regenerated Liquor Reservoir
20a------ Regenerated Liquor Reservoir Valve
21------- Amino Acid Supply Unit
22------- Electrolyte Concentrate Supply Unit (1)
23------- Electrolyte Concentrate Supply Unit (2)
24------- Manufactured Dialysate Bag (1)
24a------ Manufactured Dialysate Valve

25------- Manufactured Dialysate Bag (2)
25a------ Manufactured Dialysate Valve
26------- Pump
27------- Connector
28------- Controller
29------- Concentric Double Lumen Catheter
30------- Ventral Lateral Implanted Part
31------- Abdominal Cavity Inside Part
32------- Outer Part
33------- Reverse Flow-Proof Valve
34------- Bacteria Invasion-Proof Filter
35------- Draining Route
36------- Infusion Route
37------- Draining Route
38------- Infusion Route
39------- Pump
40-------- Computer
41------- Host Computer
42------- Controller
43------- Ventral Lateral
44------- Mensuration Meter

MOST PREFERRABLE EMBODYMENT FOR CARRYING OUT THE INVENTION

[0044] Example of regenerated liquor composition and operation procedure of the apparatus is described as follows;

(Regenerated Dialysate Composition)

[0045] The composition of the dialysate must be adjusted to minor extent to individual patient condition.,Hyper-phosphatemia, Hyper-calcemia, Hyper-magnesemia, Acidosis or Alkalosis, however most of the cases, similar composition to those listed in Table 2 can be used

Table 2

(unit: mEq /l)					
Trade Name	Na^+	Ca^{++}	Mg^{++}	Cl^-	Lactate
Dianeal					
PD 1	132	3.5	1.5	102	35
PD 2	132	3.5	0.5	96	40
PD 4	132	2.5	0.5	95	40
Perisate	132	4.0	1.0	102	35
Perisate L Ca	132	2.3	1.0	98.3	37
Peritoliq	135	4.0	1.5	105.5	35
Gambrosol	132	3.5	0.5	96	40
Gambrosol SKG	132	2.0	0.5	94.5	40
Gambrosol TCD	135	2.5	0.5	98	40

(Osmotic Pressure of Regenerated Dialysate)

[0046] Blood contains 6 to 8 gram/deciliter protein and has approximately 290mOsm/l osmotic pressure. So that for ultrafiltration, hyper-osmolar dialysate must containat minimum 8 gram/deciliter, preferably 10 gram/deciliter protein up to solubility concentration at maximum. In case needed amino acid is to be added.

The osmolality of the regenerated dialysate is to be between 300 and 500 mOsm/l.

(Usage of Regenerated Dialysate)

[0047] The selection of the osmolality for each dialysis cycle is widely variable to adjust to patient daily life. Typical example of dialysate osmolality is shown below in two cases;

Case 1			
	Storage Period hours	Osmolality mOsm/l	Use of Autocycler
1 Daytime	14	330	not used
2 Night	3	400	used
3 Night	4	330	used
4 Night	3	400	used
Case 2			
	Storage Period (hours)	Osmolarity (mOsm/l)	Use of Autocycler
1 Daytime	5	400	not used
2 Daytime	8	350	not used
3 Night	5	400	used
4 Night	6	350	used

(Regeneration Procedure)

[0048]

(1) Before sleeping at night the patient connects his catheter with the instrument, and drains the dialysate. The effluent is filtered with the pre-filter(6 and 7) and stored in the reservoir (9). The volume every time would be approximately 2 to 3 liters.
(2) Effluent in daytime is also stored in the reservoir(9).
(3) Whole liquor volume per day, 9 to 10 liter is concentrated down to below 2 liters. The filtrate, 7 to 8 liters is discarded.
(4) The concentrate is diluted with 8 liter of diluting liquor supplied from water or electrolyte supply unit (13), then concentrated down to below 2 liter in the concentrating unit (15).
One cycle of this operation reduces the residual quantity of small molecule solute approximately down to 1/5. One more cycle reduces down to 1/25.
By more times operation cycle with smaller dilution ratio, the removal efficiency is improved at same whole diluting liquor volume usage.
(5) If the patient has complication symptom, such as amyloidosis, his drained dialysate is passed through the absorption unit(8).
(6) Into the final reservoir(20), if needed, amino acid is added.
(7) Also electrolyte concentrate is added to the reservoir(20) to adjust electrolyte consistency of the regenerated dialysate.
(8) The capacity of the final reservoir (20) is to be 10 liter or more
(9) The invented instrument is equipped with auto cycling devices, pumps and valves, which is to be opened or closed by the preset computer program in the controller (28).

(Control system)

[0049]

(10) The final reservoir(20) is equipped with liquor level meter, thermometer, specific densitometer, osmotic pres-

sure meter, electrolyte consistency meter, electro-conductometer, or any other mensuration meters(44) and monitored data is memorized in the computer (40) or sent to the host-computer (41) located in hospital or control center through the public line. According to doctor's prescription, any additional order is transferred from the host-computer back to the amino acid supply unit (21), concentrate electrolyte supply units(22 and 23) through the controller (42). In daytime when the patient is away from the instrument for daily life, the instrument regenerate the dialysate automatically.

At night the instrument works as autocycler to infuse and drain the dialysate according to the preset program in the computer (40) or the order from the host-computer (41) according to doctor's prescription, by opening and closing the valves (24a, 25a)and switching on and off the pumps (5, 26) through the controller (28)

INDUSTRIAL APPLICABILITY

[0050] By the process and apparatus of the present invention, plasma protein is recovered from the effluent and reused as osmotic agent in place of glucose, consequently the adverse effect caused by glucose such as obesity, hyper-lipemia, arteriovessel sclerosis, and diabetes, can be avoided.

Dialysis therapy, i.e. removal of uremic toxin and ultrafiltration, can be achieved without problem.

By autocycler function, the patient is free from exchange operation in daytime and reduction of dwelled dialysate in the abdominal cavity make patient comfortable so that his quality of life can be improved. Also with the ancillaries, bacteria invasion is prevented so that infection rate is reduced. Lesser peritonitis and with no glucose adverse effect, peritoneum function can be maintained much longer.

With host computer located in hospital or control center, patient can be remote monitored and controlled so as to be free from complicated instrument operation. Both safeties of home therapy and patient quality of life can be improved.

Claims

1. A regeneration process of dialysate that is drained from peritoneal cavity of human body through implanted catheter and recovered which comprises

   (a) a procedure to concentrate the recovered peritoneal dialysis effluent with semipermeable membrane by one and a half times at minimum and by the extent that the consistency of the organic solute becomes not too high to be easily resolved again at maximum.

   (b) a procedure to dilute the concentrate with bacteria-free or sterile electrolyte solution by 0.5 times of the concentrate volume at minimum and by 1,000 liter at maximum once or a few times of (a) and (b) procedure repeatedly, thence

   (c) a procedure to adjust the electrolyte solution volume to add at the final dilution in order not to exceed the effluent volume

2. The recovery and regeneration process according to claim 1, wherein the aforementioned concentration procedure (a) performed with semipermeable membrane, of that maximum permeable molecule lies between 500 to 30,000 dalton.

3. The recovery and regeneration process according to claim 1 or 2, in which amino acid, albumin, or hydrolyzed protein oligomer or mixture of these substances is added to the liquor in the final dilution procedure, thence electrolyte consistency is adjusted.

4. The recovery and regeneration process according to claim 1 , 2 or 3which includes absorption procedure (d) to remove a part of solute in prior to the first concentration and/or after the last dilution procedure.

5. The recovery, regeneration and infusion apparatus of peritoneal dialysate that is infused into human peritoneal cavity, and immediately or after being dwelled or re-circulated for a certain period drained out, which includes at least a drain catheter (2), devices to concentrate the recovered effluent (11), a devices to supply electrolyte solution (13), of which one a pair of a device(11) and a device(13) or more than two sets of these are connected in a series repeatedly, and an infusion catheter (3).

6. The recovery and regenerating apparatus according to claim 5 which includes a pre-filter (6) of maximum pore size below 100 nanometer and a filter(8) of maximum permeable molecule lies between 100,000 to 1,000,000 dalton before the first concentrating unit (11).

7. The recovery and regenerating apparatus according to claim 5 or 6, which includes concentrating units (11, 15) of which semi-permeable membrane's maximum permeable molecule lies between 500 and 30,000.

8. The recovery and regenerating apparatus according to claim 5, 6 or 7 which includes a control system (f) to open and close a valve of the dialysate reservoir(20a) and valves of fresh dialysate containers (24a, 25a) following the order from a host-computer (41) in which time program of dialysis cycle and infusing dialysate volume are preset, through a computer (40) and a controller (28). and / or a control system (g) to transfer the data that is obtained by measure (44) at a dialysate reservoir (20) and its exit, to a host-computer (41) through a computer (40) and to supplement the estimated volume of amino acid (21) and concentrated electrolyte solution (22, 23) following host-computer's order(41) through a computer (40) and a controller (42).

9. The catheter used in the recovery and regeneration apparatus according to claim 5,6,7 or 8, of which the inner part comprises con-centric double lumen tube and of which one is used for infusion and the other for draining respectively and connected with the recovery and regeneration apparatus, in place of a single draining catheter (2) and a single infusing catheter (3).

10. The catheter used in the recovery and regeneration apparatus according to claim 5,6,7 or 8, of which the middle part that is implanted in patient's ventral lateral is in shape of a single smooth cylindrical tube in which two semicircle lumens leads liquor infusing through one lumen and draining through the other lumen respectively and in shape of two divided tubes in inner(31) and outer(32) parts, in place of a single draining catheter (2) and a single infusing catheter (3).

11. The catheter according to claim 5,6,7,8 or 9 of which exit of a draining tube is connected with reverse flow-proof valve(33) and of which the entrance of a infusion tube is connected with bacteria-proof filter that comprises semi-permeable membrane of maximum pore size below 50 nanometer.

Figure 1

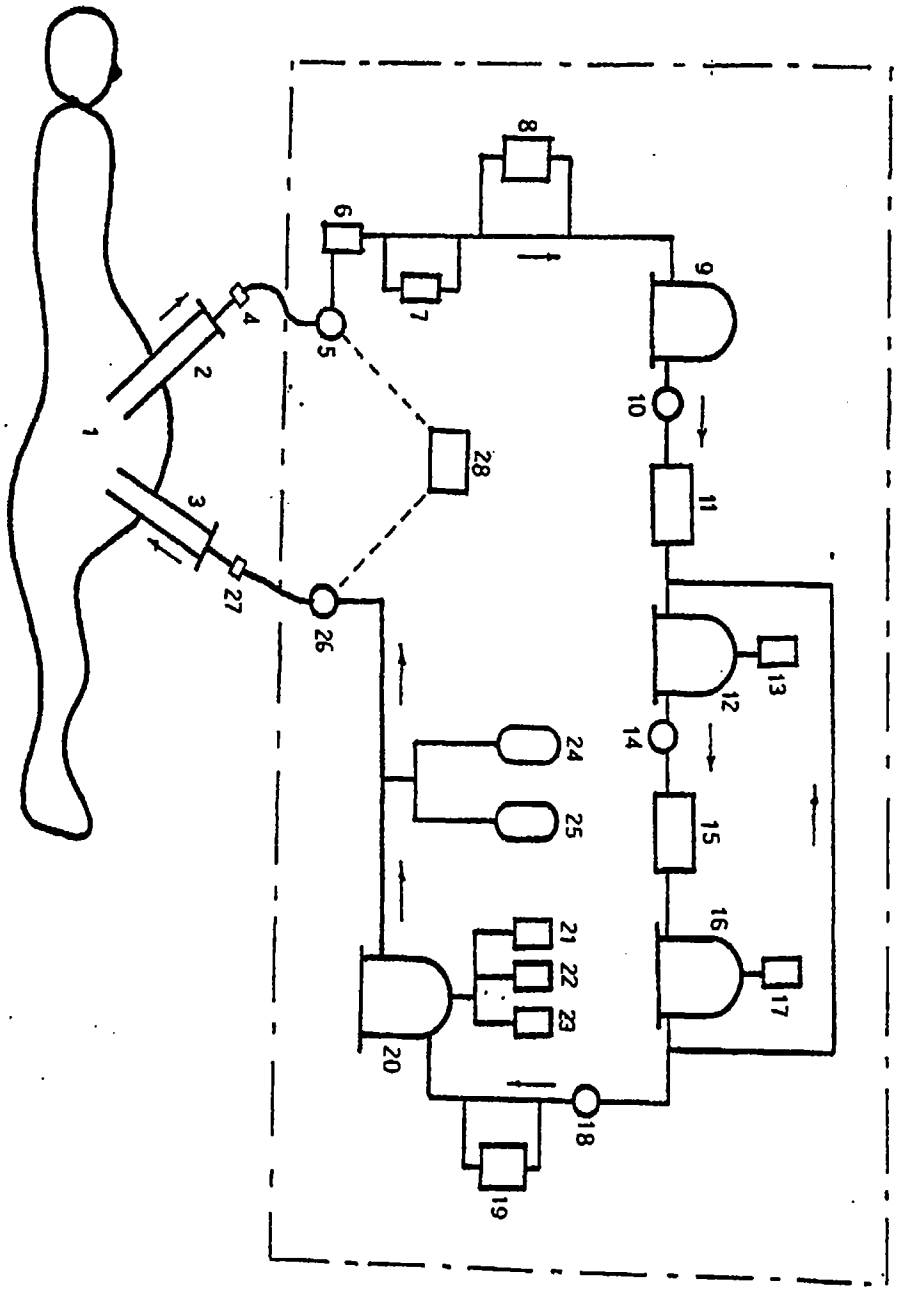


Figure 2

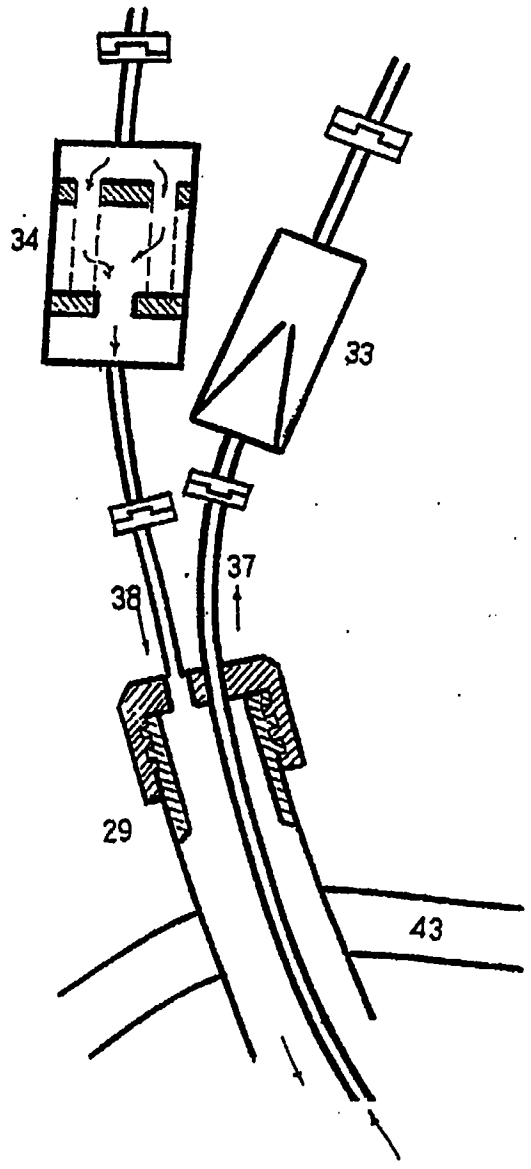


Figure 3

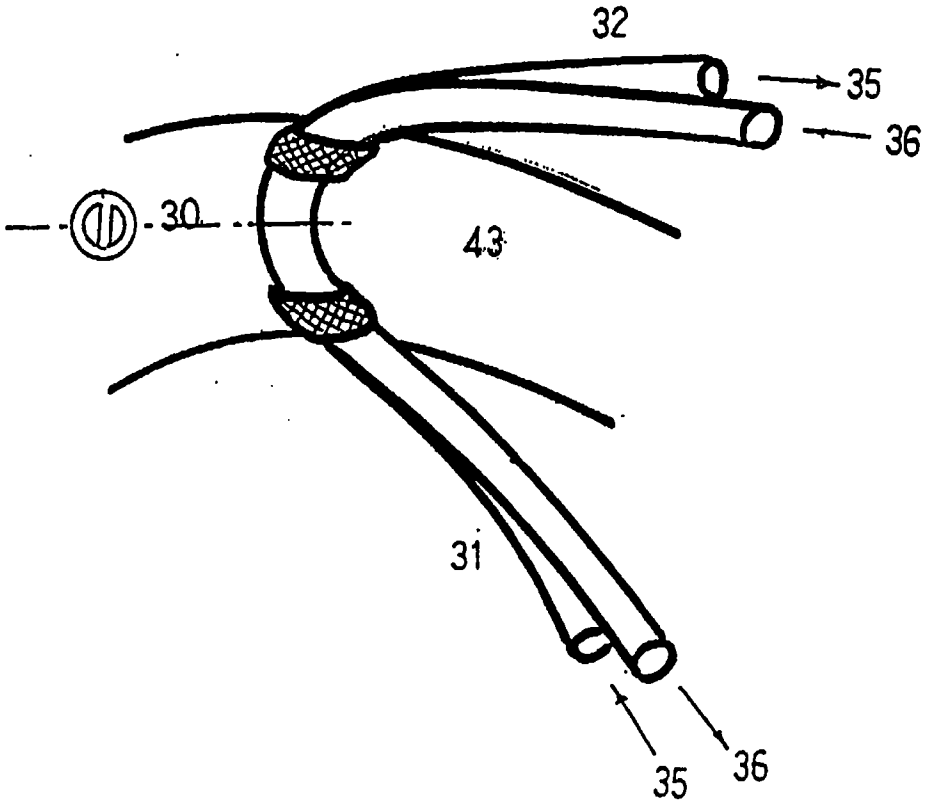
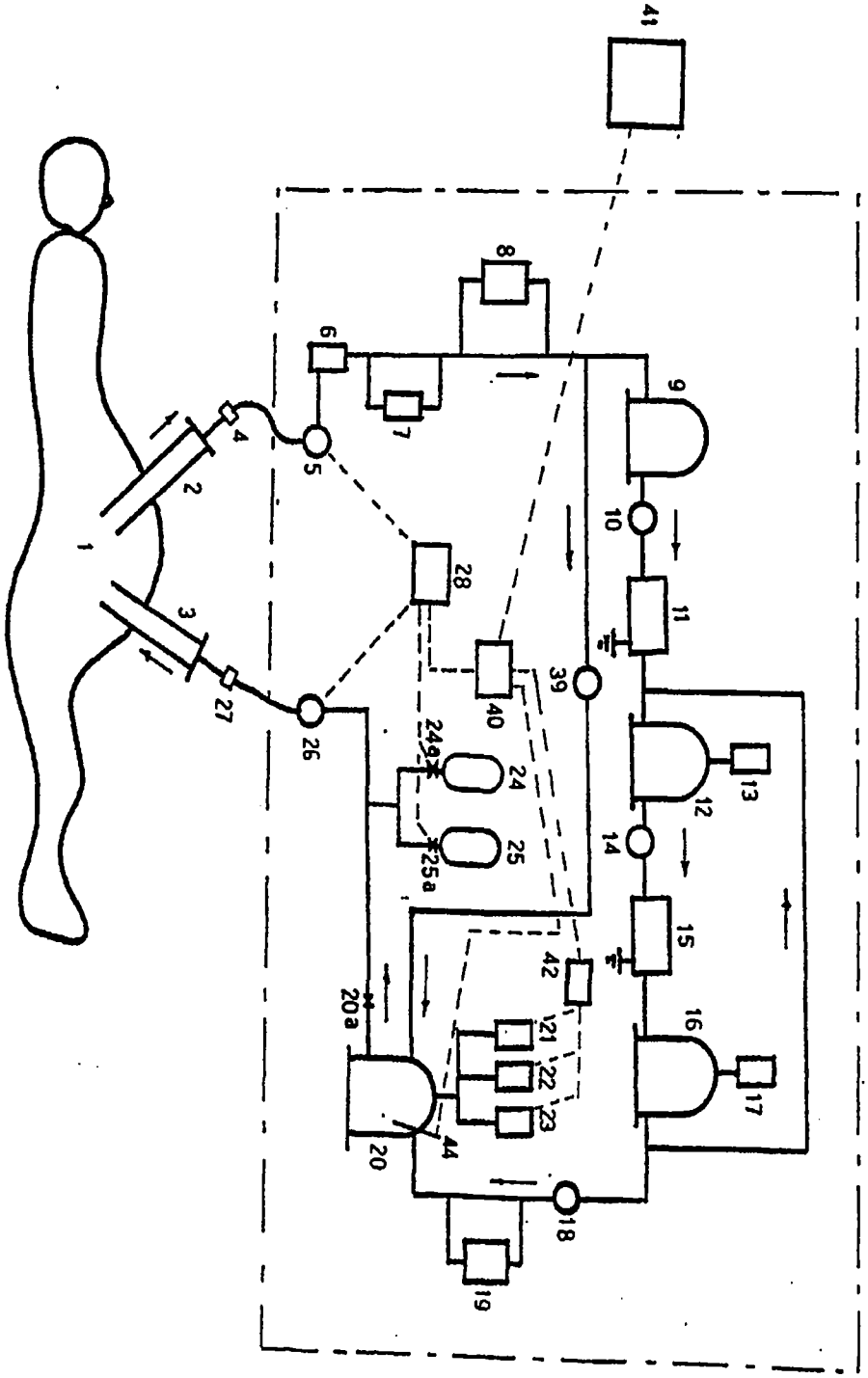


Figure 4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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP97/01950

A. CLASSIFICATION OF SUBJECT MATTER
Int. Cl^6 A61M1/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int. Cl^6 A61M1/28, A61M1/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Jitsuyo Shinan Koho 1926 - 1996 Jitsuyo Shinan Toroku Koho 1996 - 1997
Kokai Jitsuyo Shinan Koho 1971 - 1997
Toroku Jitsuyo Shinan Koho 1994 - 1997

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P	JP, 08-337590, A (Terumo Corp.), December 24, 1996 (24. 12. 96), Claim 1 (Family: none)	1 - 7
A	JP, 04-327857, A (Nissho Corp.), November 17, 1992 (17. 11. 92), Claim 1; Fig. 1 (Family: none)	9

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
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Date of the actual completion of the international search	Date of mailing of the international search report
September 2, 1997 (02. 09. 97)	September 17, 1997 (17. 09. 97)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)